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VACCINATION AGAINST INFECTIOUS DISEASES

A Conference on the Control of Infectious Diseases through Vaccination Programmes was held in October 1959 in Rabat, Morocco, by the WHO Regional Office for Europe. Its purpose was to examine different vaccination systems, experience of vaccination in the control and eradication of infectious diseases to date, and future possibilities in this field. The article that follows is based on some of the papers presented at the Conference.

Vaccination practices in Europe

Legislation on vaccination

All countries in the European Region have their own laws on vaccination, which vary considerably with political and administrative systems. For example, in Switzerland and Austria the responsibility in this respect rests with the cantonal and local health authorities only, not with the central government as in nearly all the other countries.

There are also variations in the degree of compulsion: in some countries vaccination is obligatory and fines are imposed for failure to comply with the regulations, while in others it is optional. In most cases, however, there is a mixed system: vaccination against certain diseases is compulsory, against others not.

Among compulsory systems, that of Czechoslovakia may be taken as an example. In this country the following vaccinations are all compulsory and free of charge: routine vaccinations against tuberculosis, diphtheria, tetanus, whooping-cough, smallpox and poliomyelitis; special vaccinations for persons particularly exposed to infection because of their work; special vaccinations carried out when there is a threat of an epidemic.

Mass vaccination programmes

Mass vaccination is carried out in nearly all European countries, but methods vary a good deal. In some (generally very large) countries short campaigns are organized by the central health authority with mobile teams. At the other end of the scale are the countries with permanent local services. As a rule, vaccination campaigns are based on morbidity and mortality statistics, sometimes supplemented by data from special epidemiological studies and serological surveys. These surveys should be extended: they are at present almost exclusively used for research.

Inspection and evaluation of the results of vaccination should be the work of a central authority. Where vaccination is predominantly optional they are often neglected.

So far, no satisfactory solution has been found to the problem of the registration of persons vaccinated. One good method is registration on duplicate cards, one copy being kept by the person vaccinated, the other filed in the place where the vaccination is performed. This apparently simple system is, however, rarely administered satisfactorily.

In Czechoslovakia, great efforts have been made to solve the problems of a total mass vaccination programme, and for this reason the organization of its services is of interest.

First of all, there is a centralized health system which ensures uniformity in the execution of programmes. It also facilitates continuity of control which, in order to be effective, must and does include: laboratory control of the quality, effectiveness and safety of vaccines and sera (the State is responsible for control of and research on sera and vaccines); epidemiological control of the effectiveness of sera and vaccines in large-scale use; control of the number and periodicity of vaccinations.

There is double registration of vaccinations. One record is kept in child health centres in the children's health cards, which are later passed on to the schools, places of

employment, etc. (with the exception of records of vaccination against tuberculosis, which are kept in special centres). Another record (certificate) is kept by families and all vaccinations are entered in it. This record must be produced whenever children attend for a new vaccination.

The vaccination records are subsequently inspected by the vaccinating doctors, the district medical officers and the regional medical officers. They finally reach the chief medical officer of health, who compares the data from the different regions with the information on the age composition of the population supplied to him by the National Statistical Office. The frequency, dates and times of vaccinations are also checked.

Financing of vaccination programmes

With very few exceptions, the costs in countries where vaccination is compulsory (and frequently in those where it is optional) are borne in their entirety by the central and local authorities. Some vaccines, e.g., poliomyelitis vaccine, are not usually, however, distributed free of charge, but in spite of this the demand is considerable.

In most European countries vaccines are prepared in non-profit-making State laboratories. In others they are produced by private laboratories which then sell them to the State; while in still others both these systems are in use.

Health education and mass vaccination

In 1955 an experiment carried out in two villages in Yugoslavia showed very clearly how effective health education can be in preparing the public for mass immunization campaigns. It was announced that vaccination against diphtheria and smallpox would not be compulsory that year. Instead of the distribution of the usual cards containing a reminder that vaccination was compulsory and that there were penalties if it was not done, a series of talks and personal contacts was organized a week before the date fixed for the commencement of vaccination. The local doctor explained the aims of the campaign to small groups of people who then discussed it in their homes. The result was that 92% of the children due to be vaccinated attended, whereas in the years of compulsory vaccination the average attendance had been 88%.

Without entering upon the very controversial topic whether vaccination should be voluntary or compulsory, it may certainly be said that, ideally, a vaccination programme should be carried out with the full understanding and co-operation of everyone concerned, even when vaccination is compulsory. This can be achieved by means of health education. There is no universally applicable method of health education: a careful study of local conditions must be made and the health education programme adapted to them. Among the most important local conditions to be taken into account are the economic situation, religious and social customs, and the attitude of the inhabitants to the health problem in question.

Methods of health education can be classified into two main groups: lectures, films, radio talks, television features, etc. in which the persons to be educated take no active part and whose effectiveness is for that reason very limited; methods which demand the active participation of the persons to be educated, such as discussion groups, committees, interviews, etc. These are more effective, but take more time.

In short, it may be said that health education of the public can be the decisive factor in the success of a mass vaccination campaign, provided the health educators themselves are suitably specialized and have thorough knowledge of teaching methods, so that they can at any moment suit the method to the circumstances.

Effectiveness of vaccination

This depends upon the quality of the vaccine and the conduct of the campaign. A series of laboratory and practical tests is also required, to assure the effectiveness of some of the vaccines in use. Problems continually arise in connexion with nearly all the vaccines used at present, and these require a quick solution. They are sufficiently important and varied to justify separate study of each of the chief vaccines now in use.

Recent contributions to preventive vaccination

Vaccination against tuberculosis

Although BCG is still the vaccine used everywhere against tuberculosis, some countries are preparing vaccines from murine bacilli. However, these products are still in the experimental stage. In Italy, an anti-tuberculosis vaccine prepared from killed bacilli is used, but it is confined to that country. Increasing interest has been shown in freeze-dried vaccine ever since its introduction in 1946, and it is now used in many countries, especially in the tropics. Some recent studies have, in fact, shown that a good freeze-dried vaccine gives as high a rate of tuberculin conversion as the fresh vaccine, although little is yet known about the duration of allergy after administration of dried vaccine.

The intradermal method is the most widespread, although the multipuncture technique is also sometimes used. At present there is great interest in the method of repeated oral administration of large doses of vaccine, but more information is needed for a reliable evaluation of this method.

It is agreed that vaccination should be performed at the time when the subject is most exposed to the risk of infection. In countries where tuberculosis is very prevalent vaccination should be performed at birth and subsequently repeated. In countries where it is less prevalent children can be vaccinated when they leave school or take up an occupation in which they would be particularly exposed.

Pre-vaccination tuberculin testing is considered necessary in order to prevent the Koch phenomenon. It is not essential, however, to apply post-vaccination testing to everyone: it is sufficient to test sample population groups.

Vaccination against poliomyelitis

At present, two distinct types of poliomyelitis vaccine are available, both capable of conferring active immunity; they are formaldehyde-inactivated vaccine and live attenuated vaccine.

Immunization with inactivated (Salk) vaccine. Considerable experience has already been acquired with this type of vaccine. The most generally accepted procedure is to give two or three 1-ml doses of vaccine, subcutaneously or intramuscularly at intervals of four weeks, followed by a booster dose 8-12 months later. In some countries the intradermal method has been used, chiefly when the vaccine has been in short supply, but in nearly all cases the other routes of administration have been adopted when adequate amounts became available. It cannot yet be definitely affirmed that further booster doses are necessary, although there is evidence suggesting that antibody titres are on the wane two or three years after the last booster injection. The present procedure is to carry out primary immunization between the sixth and eighth months of life, as this is the moment when the level of antibodies—both maternal and acquired—is lowest.

Space does not permit enumeration of all the studies that have been made to date to prove the effectiveness of this type of vaccine. Some very interesting figures obtained in Ontario during the 1957 epidemic were cited at the Conference: 17 cases of paralytic poliomyelitis were observed among 1 800 000 children vaccinated, as against 21 cases among 300 000 unvaccinated children. Similar results have been reported from many other countries. However, it is unanimously agreed that there is no hope of eradicating poliomyelitis by this kind of vaccination in its present form.

Immunization by live attenuated vaccine. The basic problem of this type of vaccine is the need to ascertain the extent of immunity and its duration, that the virus obtained is free from paralytogenic properties, that when it is excreted by the vaccinee and spreads among contacts it does not develop such properties, and that the virus used is capable of immunizing the subject.

The trials made so far have not always been carried out under conditions productive of reliable conclusions. But large-scale vaccination carried out in Singapore is of special interest, in that no accident occurred which could directly or indirectly be attributed to the use of the vaccine. Also of great interest are the campaigns conducted in various parts of the Soviet Union, Poland and Czechoslovakia (see article on page 142).

Vaccination against influenza

The most important problem in the manufacture of influenza vaccine is the constant antigenic variation in the virus.

It was found that some people alive during the 1889-1890 influenza epidemic possessed antibody against the 1957 Asian type of influenza. It has therefore been suggested that antigenic characteristics of the virus may be expected to reappear after about 70 years. If, as is thought, an important antigenic change occurs every 10-12 years, such as the appearance of a new sub-group, then six to seven such changes can be expected in 70 years. If this hypothesis is correct, then, since at the present time there are three sub-groups, it will be necessary to wait for the appearance of three or four new ones until a vaccine can be manufactured which will contain all the viruses representing the most important antigenic variations. Apart from the fact that this hypothesis is very tentative, there also remains the fact that a vaccine with so many components might have too weak an effect against a virus corresponding to one of them. It must therefore be admitted that vaccination against influenza cannot be considered as an effective control measure at present and that it is not likely to be so in the near future.

The vaccine prepared from live attenuated virus does not seem to give any better results than the usual type produced from inactivated virus. In the USSR, where live vaccine has been used, a reduction in morbidity of 50-75% has been reported. Among persons vaccinated by inhalation of the virus in the form of an aerosol, 5-10% showed general toxic reactions. This type of vaccine is not suitable for children under 10 years of age owing to the high incidence of febrile reactions.

A number of interesting immunological problems await solution. In principle, it would seem that circulating antibody can hardly be responsible for protection, since viraemia is unknown in influenza.

On the other hand, after both natural infection and vaccination, neutralizing antibody has been detected in the nasal secretions, and it probably exists on the surface of the entire respiratory tract. It is very likely that this surface antibody determines the degree of protection, in spite of the fact that it does not represent more than about 3% of the circulating antibody.

If the vaccine is administered by the intranasal route, a higher concentration of surface antibody is obtained, but epidemiological studies have not shown that the vaccine has any greater protective power when administered in this way.

A very interesting observation was made recently to the effect that immunity of the alveolar cells in experimental animals (ferrets) lasts longer than that of the cells of the upper respiratory tract. Intranasal instillation of a pneumotropic strain of influenza virus in an immunized animal may cause infection of the upper respiratory tract without symptoms of pneumonia. This is particularly important in human immunization, for in a large proportion of deaths from influenza the immediate cause is virus pneumonia, with or without secondary bacterial infection.

Vaccination against typhoid and paratyphoid fevers

In spite of the fact that vaccine against typhoid fever has been used for a long time, no strictly controlled epidemiological trials were carried out until quite recently.

The first practical controlled test started in 1953 in Yugoslavia, under the auspices of WHO. The subjects for the experiment were divided into three comparable groups: one group received alcohol-killed, alcohol-preserved vaccine of the Felix type; the second was given heat-killed, phenol-preserved vaccine; and the third was given an inert vaccine (placebo). The Felix-type vaccine conferred little or no immunity, but the heat-killed, phenolized vaccine was found to be effective, especially in young persons. In all, some 70% of the vaccinees were protected. This experiment also showed that it was sufficient to administer booster injections every three to four years—a particularly important point in view of the fact that these injections usually provoke stronger reactions than the primary vaccination.

Summing up, it may be said, on the basis of present knowledge, that vaccination against

typhoid is advisable in places where the disease is endemic. Nevertheless further laboratory studies and field trials are necessary before a definite conclusion can be reached about the relative effectiveness of the different vaccines and the best means of applying them.

The effectiveness of vaccination against paratyphoid fever has never been satisfactorily proved, although some recent studies seem to indicate that, in particular, the vaccine against paratyphoid A is useful although much less so than antityphoid vaccine. Further studies, with adequate controls, are necessary before any final conclusions can be drawn.

Vaccination against brucellosis

Since brucellosis prophylaxis with vaccine prepared from killed bacteria has not been very successful, a vaccine has been produced from attenuated *Brucella* strains.

A vacuum-dried live vaccine is at present being used in the Soviet Union. It is prepared in a concentration of 500 000 micro-organisms per ml for subcutaneous injection, and in a ten times higher concentration for scarification.

Vaccination against brucellosis can be more effectively carried out in regions where occupational brucellosis is more common than brucellosis of alimentary origin. Since the introduction of mass vaccination in the Soviet Union, the over-all incidence of brucellosis has decreased by some 60%. The decrease has been mainly in occupational brucellosis, which at present is 3.3 times less frequent among veterinary workers and between 7 and 8 times less frequent among shepherds; it has disappeared altogether amongst workers in the meat industry. Very significant is the fact that in the Kirghiz Soviet Socialist Republic, 1111 cases were notified in 1952 and only 33 in 1958.

Through the initiative of public health services in the Soviet Union both large and small horned livestock have been vaccinated with live vaccine from 1955 onwards. It is as yet too early for definite conclusions about the effectiveness of this method.

Vaccination against diphtheria, tetanus and whooping-cough

In many European countries diphtheria is still a considerable problem, and in some pertussis and tetanus are perhaps greater problems than poliomyelitis.

Potent antigens for immunization against diphtheria and tetanus have been known for a long time. They should be used adsorbed either on to pertussis vaccine or on to an alum preparation. If the right antigens are used in the right age groups and a sufficient proportion of the population is vaccinated, these diseases can be brought under control, as has been shown clearly with diphtheria in many countries.

A good pertussis vaccine gives 80-90% protection for several years. It should be used early, as up to 70% of deaths from pertussis occur in the first year of life. It should not be used to vaccinate school-age children because of the severe reactions. The local or general reactions that occur in 50-70% of children are not a contra-indication to immunization programmes. Convulsions are a rare hazard, and much rarer is encephalopathy, with symptoms appearing within 24 hours of the inoculation.

Active immunization against tetanus should replace antitoxin administered prophylactically. Tetanus vaccine is cheap and potent. Immunization of the mother during pregnancy may be carried out to prevent neonatal tetanus, but further investigations in this field are required. Proper individual records are of great importance with this vaccine.

Vaccines against diphtheria, tetanus, and pertussis may advantageously be used in combined form for immunization in early childhood.

Immunization programmes recommended

The Conference suggested two model schedules, one for areas with well-developed medical services, the other for areas with inadequate medical services. They cover five diseases: smallpox, diphtheria, pertussis, tetanus and poliomyelitis. Requirements vary greatly for tuberculosis and typhoid fever be-

tween different countries, so that a model schedule of immunization against these two diseases cannot be laid down.

The schedules recommended are as follows:

(*a*) *For areas with adequate public health medical services (to be modified as required to suit local conditions)*

Age	*Proposed schedule*
2-6 months	Diphtheria - pertussis - tetanus triple vaccine: 3 doses with 1 month's interval between each dose
6-7 months	Smallpox vaccination
7-10 months	Poliomyelitis vaccine (inactivated): 2 doses with 1 month's interval
15-18 months	Booster dose of triple vaccine; simultaneously, third dose of poliomyelitis vaccine
2-4 years	Fourth dose of poliomyelitis vaccine
5-6 years	Booster dose of diphtheria-tetanus vaccine; simultaneously, smallpox revaccination
10-15 years	Booster dose of diphtheria-tetanus vaccine if Schick test positive: no injection of diphtheria prophylactic in Schick pseudo-reactors

Tetanus. An individual who has been effectively immunized with a primary course of tetanus toxoid followed by 1 or 2 booster doses should be given a further dose of tetanus toxoid if exposed to the risk of tetanus. If the injury is extensive, a dose of tetanus antitoxin should also be given. If tetanus antitoxin is given to a non-immunized individual, active immunization with tetanus toxoid should be begun 4 to 6 weeks later.

Poliomyelitis. The use of live attenuated poliovirus vaccine is not included in this schedule because of the still limited knowledge about its efficacy when given orally to infants. This procedure may become the method of choice in countries where there is a high incidence of clinical disease in early infancy. In these countries immunization with inactivated vaccine may have to be begun earlier than suggested in the schedule, but in such circumstances the antibody response will be negligeable in a considerable proportion of infants because of the presence of maternal antibody.

It is suggested that the fourth dose of poliovirus vaccine be given within 1 to 2 years after the third dose of the primary course since (*a*) antibody titres may have fallen to low levels by that time, and (*b*) clinical disease has occurred in children after three doses. If the polio antigens, particularly types 1 and 3, are improved, it may be possible to postpone the fourth dose until school entry.

Quadruple vaccine (DPT and polio) is not recommended at present.

(*b*) *For areas with inadequate medical services (to be modified as required to suit local conditions)*

Age	*Proposed schedule*
3-6 months	Smallpox vaccination and simultaneously first dose of triple vaccine with alum Second dose of triple vaccine 1 to 3 months after first dose
5-6 years	Booster dose of diphtheria-tetanus vaccine; simultaneously smallpox revaccination

It is envisaged that schedule (*b*) will be used in countries with a low incidence of clinical poliomyelitis. In such areas poliomyelitis vaccine should not be employed routinely, but should be available to those at special risk of clinical disease.

Smallpox and triple vaccine should not be given simultaneously to infants with a history of convulsions or other evidence of central nervous system disease or to those convalescing from an acute infection.

The injection of an alum-containing mixed vaccine carries a slight risk of favouring the development of poliomyelitis in young children. It is recommended that the content of aluminium hydroxide or phosphate should not exceed 2 mg/ml and that the mixture should not be given to infants over 6 months of age.

LIVE POLIOVIRUS VACCINE

" The past year [1958] may truly be referred to as the international live poliovirus vaccine year, since never before have investigators from so many different parts of the world combined their efforts and facilities to obtain an answer to a question of international public health importance."

ALBERT SABIN.[1]

Millions of children and young adults have been vaccinated against poliomyelitis in recent years by means of formalin-inactivated poliovirus—the Salk vaccine—administered subcutaneously. Under the action of the formalin the virus loses its infective properties and ability to multiply, but retains a capacity to stimulate antibody formation in the organism and therefore to confer protection against the disease. This protection has proved satisfactory, since in numerous countries where large groups of the population have been vaccinated, it has lessened the number of paralytic cases. However, its efficacy is probably of limited duration and might not be enough to ensure the general protection of the population at risk in a serious epidemic.

An ideal vaccination should confer the same degree of immunity as is given by the natural disease but without producing untoward side effects. Vaccinations against smallpox and yellow fever are the stock examples of effective protection against virus diseases with risks reduced to a minimum. Researchers have accordingly, for several years past, aimed at producing a poliovirus vaccine which, unlike the formalinized product, would be living and which would multiply in the organism, stimulate the formation of antibodies, and confer protection to the same degree as a natural infection. By selection of the plaques produced by virus colonies on tissue cultures, the viruses with the most attenuated paralytogenic properties were sought, so that no danger would be involved for those vaccinated. A vaccine of this kind has the advantage of being administered orally and thus of being more convenient for systematic mass immunization.

The virus of poliomyelitis is one of those enteroviruses of which more and more are being discovered, some being recognized as pathogenic, though the disease-causing role of others is still uncertain. Paralytogenic polioviruses are able to invade the central nervous system, and by their pathogenic effect on the cells to bring about various degrees of paralysis. The virus multiplies in various parts of the body—Peyer's patches, the tonsillopharyngeal tissue or the lymph glands —although this does not determine the site of the visible lesions. Viraemia may be more or less marked, and its role in infection and immunity is still a moot point.

Live poliovirus vaccine taken orally, in liquid form or as capsules containing liquid, passes back into the intestines, develops there, and is then excreted in the stools and possibly in the pharyngeal secretions. In communities where children live in close contact, these excreted viruses will pass from one child to another, and a phenomenon unique in the history of vaccination can then be observed —a natural " serial " immunization spreading from *one* vaccinated child to *several* other children. This would be an undoubted advantage if one could be certain that the vaccine viruses will remain attenuated, i.e., that, after passing into the intestines and no longer being subject to human control, they will not regain virulence and become dangerous pathogenic agents at large in the population.

The fear that this might happen was voiced after studies in various countries had indicated that the viruses excreted by vaccinated persons were of a higher degree of neurovirulence

[1] Pan American Sanitary Bureau (1959) *Live poliovirus vaccines*, Washington, D.C., p. 14

for monkeys than the vaccine virus. However, the authors reported no evidence of progressive increase in neurovirulence for monkeys during prolonged multiplication in the vaccinated individual or after serial passage of virus in human beings.

How can we be certain of the stability of the vaccine viruses? How can we distinguish in the laboratory between the vaccine virus and the various enteroviruses or possible variants of the original virus? How can we assess the degree of protection conferred? What is the role of the other enteroviruses, and what happens when they co-exist in the intestines or tissues with the poliomyelitis vaccine virus? To answer these questions, exchange experiences and compare results, a group of eminent specialists, i.e., those who "created" the attenuated vaccine, tested it, and took the responsibility of using it in practice, met at the First International Conference on Live Poliovirus Vaccines, held in Washington, D.C., from 22 to 26 June 1959, under the auspices of the Pan American Sanitary Bureau, the World Health Organization and the Sister Elizabeth Kenny Foundation.

The detailed report on these discussions and an account of some 20 vaccination campaigns in 15 countries have just been published in a volume entitled *Live Poliovirus Vaccines*.[2] In addition, a newly published issue of the *Bulletin of the World Health Organization* contains several important articles on live poliomyelitis vaccines and, in particular, accounts of certain mass campaigns carried out with the assistance of the Organization.[3]

Vaccination campaigns

In 1957, the WHO Expert Committee on Poliomyelitis considered that studies had reached a stage at which large-scale trials in man were indicated in cases where special epidemiological conditions existed, e.g., where a population was threatened with an epidemic, or in endemic areas where there were signs of a shift to the epidemic form of the disease. The Committee recommended that the vaccines used should have given proof of their harmlessness in laboratory tests on monkeys and should have been tested also on small groups of people. Thus, during the two years preceding the large-scale campaigns described below, limited trials were carried out in family groups and children's homes in the United States of America (Louisiana and Minnesota in particular), the Netherlands, Poland, Sweden and the USSR. Then larger groups were vaccinated: 3000 children in Mexico, about 150 000 in Czechoslovakia, and 200 000 in Singapore. In Louisiana it was found that the transmission of the viruses from vaccinated persons to contacts was much more frequent in groups of persons at a low social and economic level (51% of household contacts infected) than among groups in which hygiene was better (8% infected). Several attenuated vaccines were used, particularly the Sabin, Koprowski and Lederle vaccines.

The USSR [4]

In 1956 the attenuated Sabin virus was studied in monkeys at the Institute of Virology in Leningrad. In 1957 it was administered to 150 infants and in 1958 to 2500 children under school age. In view of the strong evidence in favour of its harmlessness and efficacy, the USSR Ministry of Health then authorized general use of the vaccine and by the end of May 1959 it had been administered to several million children in various republics of the USSR. In describing these experiments at the Washington Conference, Smorodintsev and his colleagues emphasized that the vaccine stored in the frozen state at $-12°$ or $-15°C$ is extremely stable and that its activity is maintained at the same level for one to two years. The vaccine used contains 100 000 tissue culture infective doses ($TCID_{50}$) per 0.1 ml. It is administered by means of a dropper. The vaccination schedule consists of the consecutive administration of virus types 1, 3 and 2 at intervals of three to four weeks, or of administration in two stages: first type 1, then a month later types 2 and 3. Under these conditions the percentage of serological reac-

[2] Pan American Sanitary Bureau (1959) *Live poliovirus vaccines*, Washington, D.C.

[3] *Bull. Wld Hlth Org.*, 1960, 22, 197

[4] See also page 142.

tions to type 1 is 95, to type 2, 80, and to type 3, 75. If under this schedule the antibody titre falls after a time to an unsatisfactory level, the three types of virus can be administered again a year later.

The viruses multiply well in the intestines and reach high concentrations in children without antibodies in their blood. They are found in the intestinal contents on the day following administration and reach maximum titres on the seventh to fourteenth day. They may be excreted for as long as 50 days. The intensive reproduction of the viruses and their excretion lead, as explained above, to extensive spread of the vaccine virus. In a specific case described by the Soviet workers, 50% of the non-vaccinated contacts had become virus carriers within 30-50 days of the vaccination. In the majority of these virus carriers, contamination by contact had led to antibody formation. The Soviet authors furthermore declared that the most important feature of the live vaccine is its ability to stimulate the development of local immunity in the intestinal canal. Thus, when the same type of virus is administered to vaccinated children six months after the primary immunization, it multiplies only to a small extent and slowly. This form of immunity, about which little is yet known, requires further study.

Léopoldville (Belgian Congo) [5]

Paralytic poliomyelitis is endemic and epidemic in Léopoldville. Rodhain studied it there as long ago as 1919. Since 1951 there have been on the average 58 new cases a year —a rate of 18.8 per 100 000 inhabitants. More than 90% of cases have occurred in African children under 3 years of age. Encouraged by the success of vaccination campaigns, which in 1957 covered some 250 000 inhabitants of Ruanda Urundi and other territories in the Belgian Congo, it was decided to vaccinate the most susceptible population group in Léopoldville, i.e., African children under 5 years of age. For various reasons, this city was particularly suitable for testing the harmlessness of the vaccine and for studying the virus. In the Ancienne Cité, 125 000 Africans live in conditions of overcrowding and poor hygiene which favour the passage of the virus from one child to another. Furthermore, 21.7% of the city's African inhabitants fall within the susceptible age group. In addition, the health services and hospitals are excellent and ensure that the results of vaccination are conscientiously assessed. The vaccinations were carried out in community centres, dispensaries, schools or well-baby clinics, or at the Wanson Institute, where every inhabitant of Léopoldville has to undergo an annual examination for sleeping sickness, tuberculosis, leprosy and venereal diseases.

The vaccine used consisted of attenuated viruses of Koprowski's CHAT strain. The virus on which this vaccine is based comes from the fourth human passage of a virus pool of type 1 (SM). The faeces were passaged on monkey kidney culture, and then certain plaques (cytopathological lesions caused by the virus as it develops in colonies on the tissue culture) were again given several passages in tissue culture. The viruses thus obtained were remarkably attenuated, as was indicated by their lack of intracerebral and intraspinal pathogenicity.

Blood specimens were taken before and after vaccination in order to establish the percentage of children susceptible to type 1 and to all three types. By the end of April 1959 almost 46 000 children had been vaccinated, and about one in five of them had been re-examined 8-15 days after vaccination in a vaccination centre or by visiting nurses. None of the cases of illness reported among these children in the weeks following vaccination was either paralytic poliomyelitis or aseptic meningitis. Poliomyelitis was also excluded as the cause of an acute encephalitis which occurred in a vaccinated child.

The vaccination campaign had been under way for two months when an epidemic of paralytic poliomyelitis broke out in Léopoldville with 99 cases and 4 deaths, i.e., a morbidity rate of 28.6 per 100 000 (344 per 100 000 for 1-year-olds). As in previous epidemics, 90% of the cases were in the age group 3 years and under. Eighty-nine of the cases occurred in non-vaccinated children. The

[5] *Bull. Wld Hlth Org.*, 1960, 22, 203

distribution of the cases by age group was the same as in previous epidemics but, in contrast to the usual picture, cases were relatively less frequent in the Ancienne Cité. The figures are too small to furnish statistical proof of the effect of vaccination. It is not unreasonable, however, to assume that it was important, although it is possible that some unknown epidemiological factor played a part. The hypothesis of the vaccination having caused the disease in two cases in which the incubation period made this a possibility, did not, according to the authors, stand up to serological and genetic analysis, which showed that the pathogenic viruses were different from the CHAT virus.

To the surprise of the investigators the serological reaction was positive only in 60% of those vaccinated in Léopoldville, whereas in other limited population groups in the United States and Poland the serological efficacy of the CHAT strain was 90-95%. Negligence and faulty administration can be ruled out and the most plausible explanation seems to be that given by various authors who have observed similar results in regions where hygiene is not at a high level, i.e., probable interference with the poliomyelitis vaccine virus by " wild " enteroviruses normally present in the intestines of the vaccinated persons. At Léopoldville such competition between viruses seems probable, to judge from the investigation recently made there by Vandeputte,[6] who isolated enteric viruses from 37% of 1200 faeces specimens obtained during a single year from African children under 5 years of age, who were subject to epidemics of virus diarrhoea.

This phenomenon of interference between viruses contributes to a paradoxical situation in poliomyelitis protection. In environments where hygiene is at a high level and overcrowding rare, i.e., where the risks of mutual contamination are lowest, the children are not naturally protected by subclinical infections occurring when they are young, and remain dangerously susceptible to the virus. On the other hand, in communities where hygiene is rudimentary and where children contract subclinical infections at an early age and are carriers of enteric viruses, the latter can prevent effective antipoliomyelitis vaccination and hinder the formation of protective antibodies.

Andes (Colombia)

In Colombia paralytic poliomyelitis is a disease of scarcely more than minor public health importance. The highest incidence reported was 1.6 per 100 000 inhabitants in 1953. While the paralytic form of the disease is rare, poliovirus infection seems to be very widespread in certain regions of the country, to judge from the antibody level observed from the age of 2 years onwards. In the 7- to 9-year-old age group, 88% of the children have antibodies to the three types of virus, a phenomenon which occurs in other areas of the world with similar social and economic conditions.

In January 1958 cases of paralytic poliomyelitis were reported from the municipality of Andes in the State of Antioquia, in a commune which was partly urban and partly rural, situated in a mountainous area between 1000 and 3000 metres above sea level. The fear of a shift from the endemic to the epidemic form of infection impelled the authorities to undertake a campaign of vaccination with attenuated virus with the aid of the Pan American Sanitary Bureau, which serves as the WHO Regional Office for the Americas. The vaccine used was of the same strain as that which had given satisfactory and reassuring results among small groups in Minnesota. More than 7000 children were vaccinated with three successive oral doses of the three types of vaccine. Of the children serologically negative to the three types before vaccination, 91% responded to the administration of type 1, 72% to type 2 and 87% to type 3. Among those with poliomyelitis antibodies already in the blood, the vaccine had a booster effect, quadrupling the original antibody titre. The few cases of poliomyelitis reported in Andes since the campaign have not been among vaccinated children and no untoward side effects have been recorded.

It is interesting to compare the virulence of the virus used for the vaccine with that of the

[6] *Bull. Wld Hlth Org.*, 1960, **22**, 313

poliovirus causing one of the paralytic cases which led to the fear of an epidemic. While 2 $TCID_{50}$ of the pathogenic virus paralysed an intracerebrally infected monkey, more than 10 million $TCID_{50}$ of the attenuated vaccinal virus were required to cause the slightest paralytic symptom among monkeys of the same species inoculated by the same route.

Possible reversion of the attenuated viruses to virulence

Attenuated poliomyelitis viruses obtained in accordance with the principles described on page 137 are less neurotropic, or non-neurotropic, for the primates, including man. Neurotropism, however, is not a fixed and immutable quality inherent in a particular poliovirus and transmitted to the strain derived from it. It can show a wide range of variation and depends moreover on the susceptibility of the neurones with which it comes in contact. The fact that the inferior motor neurones are more highly resistant in the primates has been established beyond doubt and it seems certain that, the higher the position in the evolutionary scale, the lower the sensitivity to the poliovirus of the neurones and the higher the sensitivity of the digestive system.

The site of the test inoculation of the monkey when the neurotropic qualities of a virus are being assessed is of great importance and should be specified for comparative tests of the harmlessness of the vaccine, since monkeys show different levels of susceptibility depending on whether an intracerebral injection is made in the thalamic region or an intraspinal injection in the grey matter of the lumbar enlargement of the spinal cord.

A crucial problem arises with regard to the possibility of a reversion of the attenuated virus to virulence. How can the vaccine viruses be differentiated from " wild " viruses in faecal specimens in the absence of any distinguishing morphological characteristic, even of an ultra-microscopic kind? This question becomes acute: (*a*) when it is necessary to establish whether an attack of poliomyelitis in a vaccinated person or contact could be due to a mutation of the attenuated virus; (*b*) if the incidence of poliomyelitis increases in a vaccinated population; and (*c*) when it is proposed to vaccinate the population during an epidemic.

Sensitive serological methods, based on the inhibiting action of the specific sera of strains on virus cultures in monkey kidney tissue, have been elaborated. The specific serum prevents the formation of plaques in the case of a homologous virus and has no effect in the case of a heterologous virus.[7]

Recourse is also had to what are called genetic methods, using " markers " which appear to be stable. Among the reference characteristics for poliovirus, the following have been chosen:

(1) plating efficiency under agar of low bicarbonate content;

(2) the appearance of the plaques in tissue cultures of fresh monkey kidney and established lines of monkey kidney (the MS character);

(3) the ability of the virus to develop or not at a temperature of 40-41°C.

There seems to be a close correlation between the ability of type 1 virus to develop at a high temperature and its neurovirulence. It may even be supposed that these two characteristics are genetically identical or very closely related.

As related above, a comparison between epidemic viruses and vaccine viruses proved necessary during the Léopoldville epidemic which broke out during a vaccination campaign. Koprowski et al.[8] analysed these two viruses and showed that they were different. This analysis confirmed the indications that some characters were inherent in the attenuated forms and the contrary characters in the " virulent " forms.

Achievements and needs

It was the opinion of the Washington Conference that, while the inactivated (Salk) vaccine has proved its value and can be strongly recommended, its use does not preclude that of a less expensive and more easily

[7] *Bull. Wld Hlth Org.*, 1960, 22, 235
[8] *Bull. Wld Hlth Org.*, 1960, 22, 243

administered vaccine, which might replace the " wild " paralytogenic strains in nature by strains with lessened neurotropism. However, the fact, which in itself has certain advantages, that the vaccine virus spreads to contacts is not without its risks, since its spread cannot be controlled. These risks were discussed and assessed at length by the Conference. The neurovirulence of the vaccine virus has hitherto been considered as the factor involving the greatest risk. Other factors, however, also require study: the invasive power of the virus in the organism, viraemia in vaccinated persons, the contagious properties of the virus and its ability to spread from one person to another, its genetic stability, and the value of certain markers as criteria of infectivity permitting differentiation between " wild " polioviruses and the viruses excreted by vaccinated persons.

It remains difficult to assess the results of vaccination campaigns, particularly if a statistically valid verdict on efficacy is required. Such assessments are at present based above all on qualitative comparisons. The serological response which can be measured in important sample groups of the population has raised the question of the interference of enteric viruses with the poliovirus and of interference between the polioviruses themselves. This is a subject for wider research. The spread of vaccine viruses in communities partially immune before vaccination, which is slower than in non-immune communities, is still a matter for study. However imperfect the trials of the live vaccine made so far, nothing has arisen to suggest that it is not harmless, or to throw doubt on its effectiveness once the organism has responded by producing antibodies and excreting viruses.

LIVE POLIOVIRUS VACCINATION IN THE USSR, POLAND AND CZECHOSLOVAKIA

Live poliovirus vaccination has already been practiced on a large scale in the USSR, Poland and Czechoslovakia. With the agreement of the ministries of health in these three countries, WHO invited Dr Dorothy Horstmann, Associate Professor of Preventive Medicine and Pediatrics at the Yale University School of Medicine, USA, to visit these countries between August and October 1959 and evaluate the results of the mass vaccination programmes carried out with the live vaccine. She spent most of the time at her disposal in the USSR, and a week each in Poland and Czechoslovakia.

The USSR

Some 15 million persons were vaccinated in the USSR by the end of January 1960, and it is planned to vaccinate another 60 million by the end of the year, i.e., practically the entire population under the age of 20.

Striking features of laboratory work in this country are, in Dr Horstmann's view, the large staff available and the high standards of sterile technique. The methods used for preparing tissue cultures and for the determination of neutralizing antibodies are similar to those used elsewhere, and the laboratory work is of good quality. Some delay seemed to her to occur in the carrying out of tests, and particularly in the isolation of virus from cases, due mainly to the large number of specimens collected from areas scattered through vast tracts of country and to the absence of staff on expeditions to republics starting vaccination programmes.

The decision to undertake the vaccination programme was delayed for several months pending detailed study of the problem by the Ministry of Health, and when permission to start was given the vaccine was offered to the republics to use or not as they wished. There had been an epidemic of poliomyelitis in Estonia in 1958, and possibly for this reason this republic was the first to ask for the

vaccine. The success of the programme in Estonia set off a " chain reaction " throughout the other republics, and at the time of Dr Horstmann's report only one republic had not asked for the vaccine.

The vaccine, which is prepared from the three strains developed by Sabin, was administered serially to begin with: first type 1, then type 3, then type 2.[1] In Lithuania groups vaccinated serially in this way were compared with groups vaccinated with a triple vaccine either once or twice; and when the preliminary results showed that there was no significant difference in the two methods triple vaccine became the only one used. In Georgia the administration of triple vaccine to children in sweetmeats is being tried.

The vaccination campaign begins by enlisting the co-operation of the doctors and the public. The directors of the programme assemble the doctors and explain the organization of the programme, the role of the doctors, their responsibilities during the campaign and afterwards, and the importance of close surveillance. Radio and television broadcasts, newspapers and posters bring the aims of the campaign before the public to persuade it of the advantages of co-operation. An important town in each region is selected as a centre. To it is sent frozen vaccine, sufficient for several days of vaccination; and from it teams go out daily, carrying the vaccine in iced thermos flasks. In the rural areas these teams each consist of a medical auxiliary with some medical training (called a " feldscher ") and two nurses. In the towns teams are set up in schools, nurseries, kindergartens and out-patient departments, and a physician supervises the work of several teams. Data are recorded on every person vaccinated.

This is the system generally used, but there are slight variations between the republics. There are no control groups and no selection of persons for vaccination other than by age, for this is meant to be a mass vaccination programme, not a controlled trial of a new kind of vaccine for poliomyelitis. As in other mass campaigns, an indefinite number of people have been missed, being absent, ill, or reluctant to face vaccination; but this number was reduced by a continuous vaccination programme through the summer of 1959. Accurate population data have made the planning of the campaign much easier.

Before the vaccination began serological surveys were made to determine the immunity status of the population. The children surveyed in the age group 0-3 consisted only of those living in nurseries or staying in them during the day, a group which Dr Horstmann does not think representative of the population at large. The survey of the age group 4-7 also drew too heavily on children in institutions and in kindergartens. The group 7-14 consisted mainly of schoolchildren, and the adults surveyed were mainly factory workers. This survey work has been held up by difficulties with the colorimetric neutralization test, but these have been overcome.

Surveillance is efficiently carried out. In each area the vaccination teams are also surveillance teams. In Tashkent, for example, where the vaccine was given during an epidemic, every home was visited every 5-6 days from mid-July to mid-September 1959 to check on possible cases. Generally, however, the local paediatrician notifies a case to the area sanitary and epidemiological station, which sends an epidemiologist to the child's home to make a thorough inquiry into the case and its contacts. The Ministry of Health in Moscow has set up a special notification system for cases of poliomyelitis, and all suspicious cases (that is, all with acute infection of the central nervous system) are sent to hospital for confirmation of the diagnosis and treatment. Dr Horstmann considered that it was most unlikely that any paralytic cases would be missed under this system.

Since there are no controlled trials, the 1959 incidence of poliomyelitis in vaccinated and unvaccinated persons cannot be compared. But the over-all incidence, in comparison with the previous five years, showed a marked fall in 1959. Some of the republics attribute part of this fall to vaccination with the Salk vaccine, but this vaccine has not been extensively used.

Dr Horstmann concludes that the attenuated live vaccines used appear to have been safe, both to those vaccinated and to the

[1] For further details on this vaccine and its effects, see page 138.

communities in which they live, for at least the six-month period during which surveillance was carried out. The fall in the number of cases suggests that the vaccine is effective, although the absence of a controlled trial makes it difficult to gauge its effectiveness accurately.

Poland

Until 1951 poliomyelitis was sporadic in Poland, and of little importance. An epidemic occurred in that year, with an attack rate of 12.2 per 100 000, and an epidemic in 1958 had an attack rate of 21 per 100 000. Cases have been confined to the lower age groups: approximately 70% have been in children under 4 years of age, 95% in children under 8.

Vaccination with the Salk vaccine was begun in 1957, and in 1958, after the epidemic, extended to most children under 7. In October 1958 vaccination with the Koprowski live poliovirus vaccine was begun on a small scale. Mass vaccination with this vaccine was begun in June 1959, and by the time Dr Horstmann wrote her report nearly a million children had been vaccinated with types 1 and 3. The aim is to vaccinate the entire population with these two types, and for the moment to ignore type 2. Children who have had two doses of Salk vaccine receive a booster dose of live vaccine.

As in the USSR the health services are well organized and surveillance efficient. Vaccination is compulsory, and if parents fail to bring their children they are heavily fined. The immunity status of the population is studied before the vaccine is administered. Dr Horstmann points out that, because the population is relatively small, accurate information should be available soon on the safety and effectiveness of the vaccine.

Czechoslovakia

In 1957-1958 vaccination was extensively carried out, Salk vaccine being used. Sabin live vaccine has now been given to children who had three doses of Salk vaccine, and the trial is being well controlled. The standard of work in the laboratories in Czechoslovakia is high, epidemiological services are good, and surveillance is being carefully carried out. The incidence of poliomyelitis was extremely low in 1959.

Serological surveys were made before and after vaccination with the Salk vaccine, and before vaccination with the Sabin vaccine; and the series is being completed with a post-Sabin survey. The prevalence of poliovirus infection is assessed at intervals of 3-4 months by sampling the population under 5 years of age in both vaccinated and non-vaccinated areas. The results from the samples taken 5½ months after vaccination with the oral vaccine show that there is no significant difference between the amount of poliovirus circulating in the vaccinated regions and that in the rest of the country.

Yaws and standards of living

"It is at least suggestive that one of the main factors reducing yaws prevalence may be more water and more soap." This statement by Dr C. J. Hackett, Medical Officer, Venereal Diseases and Treponematoses, WHO Headquarters, appears in an article on epidemiological aspects of yaws eradication, which will shortly be published in the WHO Bulletin. The article explains:

"A great reduction in the prevalence of yaws not attributable to a mass treatment campaign is usually accompanied by other changes that have contributed to the raising of the standard of living. The more obvious of these are more and better clothing; more bicycles on the roads; more village schools and more secondary school places; more dams, boreholes and wells available and in use; and more soap—all of which are signs that the community is wealthier. However, village houses may be in no better state of repair, and excreta disposal may still remain a matter of individual action."

COLLECTIVE ANTIBIOTIC TREATMENT OF TRACHOMA

By the early nineteen-fifties it was clear from numerous reports that certain of the broad-spectrum antibiotics were effective against trachoma. It seemed, however, that treatment would have to be continued over long periods to cure the average case. With help from WHO and UNICEF, comparative trials have been conducted in Morocco since 1954 to assess the value of local treatment of trachoma with chlortetracycline and to develop much needed simple and economic methods of treatment suitable for mass campaigns. These trials were on a scale unprecedented in connexion with the disease, covering more than 9000 schoolchildren with active trachoma. They are reported on by J. Reinhards, A. Weber & F. Maxwell-Lyons in an article which recently appeared in the WHO Bulletin [1] and which is summarized below.

Marrakech was the first large town in Morocco where all trachomatous schoolchildren were given collective treatment with antibiotics. The schedule of treatment was that recommended in the first report of the WHO Expert Committee on Trachoma: [2] a local application of chlortetracycline in the form of a 1% ointment three times daily for 60 consecutive working days (five days each week). Some 3800 schoolchildren were treated in this way at the beginning of 1954. The results of this first treatment, observed seven months later, were as follows:

56.9% of the children were clinically cured;
33.6% showed appreciable improvement and were probably cured (these cases were classified as " Category X " pending further observation);
9.5% still showed signs of active trachoma.

During the next school year, the remaining active cases received further treatment, trisulfonamides being administered as well as chlortetracycline ointment. Following this treatment only 1.6% of the total number of children treated were still uncured. It was also found that the great majority of the " Category X " cases had been cured by the first treatment.

In the school year 1955-56, a comparative trial of three schedules of treatment was carried out in Meknès. They were:

Schedule 1—Application of 1% chlortetracycline ointment three times daily for 60 consecutive working days;

Schedule 2—Application of 1% chlortetracycline ointment twice daily for 60 consecutive working days;

Schedule 3—Application of 1% chlortetracycline ointment twice daily on three consecutive days, repeated every four weeks over a period of 20 weeks, i.e., six three-day cycles of treatment.

A total of 4136 children, divided into three distinct but comparable groups, were treated. The results given by each of the three schedules were remarkably similar in relation to stage and severity of the disease, age group, and social and economic level. Nor was there any appreciable difference between the results in respect of the degree of cicatrization after cure and the relapse rate ascertained a year after treatment ended.

In 1957-58, intermittent short-term treatment was again tried out, this time in the rural schools of the Province of Tiznit (southern Morocco). In this part of the country secondary infections are more prevalent and general living conditions are on a lower level than in the northern towns. Treatment schedules 2 and 3 were applied to two groups containing a total of 1167 children. As at Meknès, no appreciable difference was observed between the results of continuous treatment and those of intermittent treatment.

In none of these trials was an evaluation of results made until a follow-up period of four to seven months after the termination

[1] *Bull. Wld Hlth Org.*, 1959, 21, 665
[2] *Wld Hlth Org. techn. Rep. Ser.*, 1952, 59

of treatment. In addition, further examinations took place between twelve and eighteen months after the end of treatment to detect late relapses or errors of diagnosis.

The main results of the trials may be summarized as follows. The application of chlortetracycline resulted in the clinical cure of 57-80% of trachoma cases among the Moroccan children thus treated, the rate depending on the stage and severity of the disease and on the living conditions of the communities involved. Even in the more resistant cases, a very high proportion of cures was obtained after a second course of treatment. It would appear that relapse and reinfection rates are relatively low in schoolchildren, at least in the urban districts of Morocco. Clinical evidence was collected to the effect that, after appropriate treatment with antibiotics, fine papillary hypertrophy associated only with scars is not to be considered as a sign of persistent activity of trachoma. Finally intermittent short-term treatment was found to be as effective as the treatment schedule originally recommended in the first report of the WHO Expert Committee on Trachoma.

The authors suggest the following explanation of the effectiveness of intermittent treatment. The trachoma virus is probably most susceptible to antibiotics during or soon after the phase of multiplication. The three-day treatment cycle may be enough to eliminate all virus particles which have reached this stage, but not those which are in an inactive state at the time of application. Thus short treatment cycles, repeated at appropriate intervals, should eventually eliminate the virus.

Whatever the explanation, the intermittent method proved extremely effective in the treatment of trachoma in Morocco. Moreover, preliminary reports of trials in other countries confirm the finding that there is little difference between the results with this method and those with the old continuous treatment method. The use of intermittent treatment makes for great economy in antibiotics and in staff and other campaign expenses, thus permitting a wide expansion of mass treatment programmes.

The authors recognize that the minimum requisite treatment of trachoma with antibiotics may vary from country to country, and that factors such as irregular attendance may impose a treatment cycle of more than three days. They recommend that well-controlled trials be carried out in each country to determine the schedule of treatment most appropriate to local conditions and needs.

INTERNATIONAL WORK IN HEALTH STATISTICS, 1948-1958 *

9. Levels of living

In 1952 the United Nations General Assembly requested its Economic and Social Council to " provide for the working out of adequate statistical methods and techniques so as best to facilitate the gathering and use of pertinent data in order to enable the Secretary-General to publish regular annual reports showing changes in absolute levels of living conditions in all countries ". The Secretary-General convened a committee of experts to report on the definition and measurement of standards of living. This committee, which preferred the use of the term " levels of living " for actual living conditions, leaving the term " standards of living " to cover " future aspirations ", was unable to formulate a single index of the level of living, but concluded that " the most satisfactory approach to international measurement of levels of living would be through the measurement of clearly delineated aspects or parts of the total life situation

* The earlier parts of this account of WHO's work in international health statistics appeared in *WHO Chronicle*, 1959, 13, 67, 214, 253, 378, 417, 446; 1960, 14, 66, 116.

that are amenable to quantification and reflect international aims ".[1] Statistical measurements were to be sought, therefore, for twelve components of levels of living which, the committee considered, would form a satisfactory international catalogue of such aspects. Of these twelve components, " health, including demographic conditions " was placed first.

The United Nations Statistical Commission discussed the committee's report, and recommended that the specialized agencies, each in its own field, examine the adequacy of the indicators proposed by the committee, as well as the availability and accuracy of the statistics relating to such indicators. In pursuance of this recommendation a WHO Expert Committee on Health Statistics [2] examined the indicators proposed by the United Nations committee for the component " health, including demographic conditions ". These indicators are: (*a*) expectation of life at birth, (*b*) infant mortality rate, (*c*) crude annual death rate, (*d*) number of hospital beds in relation to the population, and (*e*) number of physicians in relation to the population. Each of these indicators, in the Expert Committee's opinion, has its disadvantages. The expectation of life at birth is affected significantly by the infant mortality rate, the accuracy and reliability of which are questionable in many territories of the world because of incomplete registration. Moreover, indices of expectation of life are themselves not available in many countries, especially in under-developed ones. The crude death rate is of limited value because of the influence of the sex and age structure of the population. There is no international comparability of quality of medical care facilities, so that the number of hospital beds and of physicians would not show how well equipped the hospitals are, nor how competent the physicians. In any case, hospitals and physicians tend to be concentrated in urban areas in some countries so that urban levels of medical care are higher, rural levels correspondingly lower. The Expert Committee reviewed other possible indicators, such as the number of deaths from infectious diseases in relation to all deaths, the number of deaths under five years of age in relation to deaths at all ages, and the use of morbidity statistics. However, it felt that, in view of the complex nature of the issues involved, further studies of these were required.

In October 1955 WHO convened a Study Group on the Measurement of Levels of Health,[3] which included among its members statisticians, public health experts, a social scientist, and an anthropologist.

The Group was confronted with two questions: what can be done with available health statistics as indicators (perhaps suitably refined); and can any new indicators be suggested?

In the opinion of the Group health indicators might be classified in three categories: (*a*) those associated with the health status of persons and populations in a given area (vital statistics, nutrition, etc.); (*b*) those related to physical environmental conditions having a more or less direct bearing on the health status of the area under review; and (*c*) those concerned with health services and activities directed to the improvement of health conditions (availability and use of hospitals, physicians and other health personnel).

The Group reviewed the sources available to the health administrator for measuring levels of health, such as vital and health statistics, epidemiological information, and data from surveys. None contains satisfactory specific indicators of health from the threefold aspect of physical, mental and social well-being. Nor are the techniques for measuring the level of morbidity sufficiently advanced to provide a satisfactory indicator. Mortality statistics, however, for all their limitations, have the merit of availability both from one period to another and from one country to another.

The Study Group discussed the concept of health and possible indicators of health. These might be roughly divided into those

[1] United Nations (1954) *Report on international definition and measurement of standards and levels of living*, New York (E/CN.3/179-E/CN.5/299)

[2] *Wld Hlth Org. techn. Rep. Ser.*, 1957, 133

[3] *Wld Hlth Org. techn. Rep. Ser.*, 1957, 137

based on available statistics and such new ones as might be devised. Among the former, there are comprehensive indicators, such as the expectation of life and the crude death rate, and specific indicators, such as infant mortality, deaths from communicable diseases per 100 000 population, and indicators of health services and activities. Among the latter might be considered the percentage of population receiving a protected water supply, or the percentage having facilities for proper disposal of excreta, or indicators measuring the status of mental health, nutrition and housing (as seen from its health aspect). The group weighed up the merits and demerits of each of these indicators, and concluded that further information was required. It accordingly recommended that special sampling surveys be undertaken of morbidity, nutrition, mental health, environmental factors, health services, and social and economic conditions.

In its discussions the Study Group considered the proportional mortality ratio (the number of deaths at ages 50 years and over as a percentage of total deaths) as a possible comprehensive indicator of health. In the view of the Study Group, this indicator—which was devised by WHO [4]—was a promising one, because the primary data are comparatively easy to collect and the method of construction is straightforward. It felt, however, as did the authors themselves, that further critical studies would be necessary before it could be definitely accepted. The proportional mortality ratio has now been further tested by its authors, who have produced statistical evidence to show that it satisfies certain essential conditions. These are: records should be available from as large a number of countries and territories as possible; the indicator should be related as far as possible to the country as a whole, not just to a selected area or population group; the records needed for its estimation should not be unduly affected by such defects as under-registration or differences in terminology; and the indicator should be of a comprehensive character, simple enough to command acceptance internationally, and sufficiently discriminating to distinguish between countries at various levels of health. In spite of some weaknesses, they therefore concluded that it is the most suitable indicator of " health, including demographic conditions ".

The fifth [5] and sixth [6] reports of the WHO Expert Committee on Health Statistics briefly reviewed contributions to the development of indicators of health levels. They reiterated the opinion that theoretically the expectation of life at birth, at 1 year, or at any other age is the best indicator of all; but admitted that it is available for only a small number of countries, and even then at infrequent intervals. The best practical comprehensive health indicator suggested hitherto is the proportional mortality ratio, and the Expert Committee accordingly recommended that it be explored on an experimental basis until its usefulness can be judged in the light of experience. Referring to specific indicators, the Committee emphasized the value of the infant mortality rate, and in particular the late infant mortality rate (from 1 to 11 months), because the latter is less influenced by pre-natal and intrapartum causes of death. The total death rate in the 1-4 age group was also suggested for trial as a specific indicator where accuracy of age-recording justifies its use. A choice has to be made between a series of indicators which fulfil to different degrees the criteria of statistical significance, and of availability. It is to be hoped that the work initiated by ILO and WHO on family living studies and family health surveys will provide valuable data which in future can be used for the measurement of levels and trends in health.

[4] *Bull. Wld Hlth Org.*, 1957, **17**, 439

[5] *Wld Hlth Org. techn. Rep. Ser.*, 1957, **133**

[6] *Wld Hlth Org. techn. Rep. Ser.*, 1959, **164**

TRAINING OF PERSONNEL FOR MALARIA ERADICATION

International staff

The malaria eradication programme of the World Health Organization covers almost 100 projects. In these the Organization's most important participation is the provision of experts to give technical advice in various branches of malaria eradication. In addition, senior specialists are employed in the Organization's six Regional Offices and in the Malaria Eradication Division in Headquarters.

The number of staff authorized for the whole programme is about 390, including medical officers, entomologists, engineers, sanitarians, laboratory technicians and administrative officers, as well as chemists, biologists, parasitologists, statisticians, health educators, transport officers, etc.

As the demand for personnel experienced in malaria work far exceeded world supply, it was found necessary to recruit a number of persons with suitable basic qualifications and to give them training in the modern malaria eradication techniques adopted by WHO.

For this reason training courses were instituted in various centres all over the world. So far, more than 200 people have been trained in the following centres: Kingston (Jamaica), Maracay (Venezuela), Mexico City (Mexico), São Paulo (Brazil), Tala (Philippines), Delhi (India), Amani (East Africa), Cairo (United Arab Republic), Guatemala, Amsterdam (Netherlands), Basle (Switzerland), London (England), and Rome (Italy). Courses have been held in Spanish, Portuguese, English and French.

Some of these centres, like those in London, Amsterdam, Delhi, Rome and Basle, are internationally known training institutes where courses have occasionally been held for the training of groups of WHO staff, while others, such as those in Kingston, Maracay, Mexico City, São Paulo, Tala and Cairo, are specialized malaria training centres where courses are regularly held for both international and national staff, in most cases with the help of WHO. WHO frequently provides some equipment, supplies, and transport, and contributes teaching and administrative staff. A number of other centres will be encouraged to take part in the programme in the near future to help meet the increasing demand for trained malaria staff.

Candidates for international recruitment are carefully selected with due regard to their background. Other conditions being equal, preference is given to those who already have some knowledge of, or training in, malaria work, experience of tropical life, and knowledge of English or French, or both.

The basic qualifications required for the various categories of staff are as follows: for medical officers, a degree in medicine and a diploma in public health or tropical medicine and hygiene (or both), or long experience in public health activities; for entomologists, a degree in science (entomology) with a diploma or training in medical entomology, preferably malaria entomology; for engineers, a degree in civil engineering with a diploma in public health or sanitary sciences (or both); for sanitarians, a diploma in sanitation or the equivalent with experience in public health work (preferably antimalaria work); for laboratory technicians, a diploma in medical technology or its equivalent, with several years' experience of laboratory work, preferably with some knowledge of haematology and entomology applied to malaria.

The selected candidates are sent to the training centres to learn the latest techniques advocated by WHO for malaria eradication programmes. At the end of the course, which may last from one to three months according to the category of staff, the trainees come to Geneva and are given an examination. Those who pass are offered contracts, generally for two years, and are sent to field teams for a period of in-service training. Each successful candidate is given full responsibility in a programme as soon as a satisfactory appraisal of his performance is obtained from his supervisor.

In the Americas, trainees are usually sent, after the theoretical part of the course, to

visit malaria eradication programmes in operation in the Region, e.g., in Mexico, Venezuela, Brazil, El Salvador, Guatemala, etc. In other parts of the world programmes such as those in Syria, Lebanon, Iraq and China (Taiwan) are also being used for field visits.

It is expected that a number of candidates in the various categories mentioned above will still be required in the future in malaria eradication programmes and the Organization is still actively looking for suitably qualified people. Apart from the technical criteria that have to be satisfied in the selection, recruitment, training and posting of the candidates, there is also the aptitude to become an international civil servant, without which the task in the field cannot be satisfactorily performed, however high the candidate's qualifications and however wide his experience.

National staff

A number of qualified and trained personnel are necessary to the success of any malaria programme. While it is generally not difficult to recruit such categories of staff as spraymen and it is still relatively easy to recruit and train squad leaders, it is becoming increasingly difficult to find and train staff of a higher level, including persons to serve as directors of various departments in the national malaria service and in the very important key position of director of the service itself. Engineers, entomologists, parasitologists, administrators, health educators, epidemiologists, etc., are required.

In a number of countries it is possible to find people sufficiently qualified to fill these positions in their national eradication services, after further specific training. In other countries, however, people with the required basic qualifications are not available at all.

Advanced training in specific branches of malaria is offered to national staff by WHO in the form of fellowships; a number of fellows are sent to the training centres mentioned above where the latest techniques adopted in malaria eradication programmes are demonstrated. Training of national staff is also provided for by WHO malaria country advisers. The Organization also sponsors tours and visits of national malaria staff members to other malaria programmes to observe certain aspects of field operations. In some countries training courses are organized with the help of specially recruited WHO consultants. The Organization has recently arranged for consultants to visit existing training institutions in certain countries with a view to developing them into permanent malaria training centres to serve a number of countries in the same region.

In reviewing and appraising the results of a number of malaria eradication programmes, it has been clearly brought to light that the lack of trained national staff is frequently the cause of failure in the correct implementation of field operations and that therefore no success can be foreseen if national services are not adequately staffed both in quantity and quality. WHO is therefore paying increasing attention to this aspect of malaria training.

Finally, there are the malaria conferences, seminars and symposia frequently organized or assisted by WHO. Such meetings give malaria workers of various countries the opportunity to exchange ideas and benefit from the experience of others. Under the programme of exchange of scientific workers, the Organization invites a number of national malaria workers of a high level to visit malaria eradication programmes in other countries so that they may exchange ideas and discuss experiences with local malaria officials on the spot.

Opportunities for training in malaria work

Medical and technical personnel interested in taking part in malaria eradication work in any of the categories mentioned in the above article are invited to write to the Chief of Personnel, World Health Organization, Palais des Nations, Geneva, Switzerland, quoting the reference: WHO Chronicle (April 1960).

EXECUTIVE BOARD : TWENTY-FIFTH SESSION

The Executive Board of WHO met from 19 January to 1 February 1960, in Geneva, under the chairmanship of Professor E. J. Y. Aujaleu (France). The Vice-Chairmen were Professor N. Etemadian (Iran) and Dr M. M. Penido (Brazil). Dr D. Castillo (Venezuela) and Dr A. J. Metcalfe (Australia) were Rapporteurs. A wide range of technical, financial and administrative items were discussed. Certain questions of general interest are reviewed below.

Programme and budget for 1961

The Board unanimously recommended the adoption by the World Health Assembly of a working budget of $18 569 620 for 1961. This represents an increase of about 10% over the figure for 1960, reflecting the growth of the Organization's activities, particularly in the eradication of communicable diseases, medical research, the improvement of environmental sanitation, and the education and training of health personnel.

Medical research

A report to the Board on the general development of the intensified medical research programme was based on the recommendations of the WHO Advisory Committee on Medical Research composed of a number of eminent scientists, each a recognized authority in his field. The subjects dealt with were: malaria, tuberculosis, treponematoses, leprosy, onchocerciasis, bilharziasis, virus diseases, insecticide resistance and vector control, veterinary public health, antibiotics, cancer, cardiovascular diseases, radiation and genetics, and biological standardization. It was recommended that priority be given to: services to research such as the standardization of nomenclature, techniques and equipment to ensure comparable results in different parts of the world; setting up reference centres for the identification of micro-organisms, tissues, etc.; improving the training of research workers and communications among them. Next in priority would come demographic studies into the varying incidence or prevalence of diseases, and international coordinated research programmes that might have a bearing on major WHO programmes. The Board noted these priorities and expressed its satisfaction with the proposed research programme for 1960 and 1961.

The Board considered a United Nations resolution on the international encouragement of scientific research into the control of cancerous diseases through the award of prizes for outstanding work in this field. The Director-General was asked to study with the Secretary-General of the United Nations the best way in which to award prizes, but, in the light of the world-wide study made by WHO in connexion with the intensification of its medical research programme, the Board doubted whether awarding prizes was the most suitable means of encouraging medical research.

Malaria eradication

An interim report was presented on the development of the world-wide malaria eradication programme; a more comprehensive report of progress in 1959 will be submitted to the Thirteenth World Health Assembly. Judging by the number of campaigns planned or in operation, the programme was progressing satisfactorily. Eradication operations were under way in 65 countries and territories, and 33 countries and territories had realistic plans for initiating them. Many hundreds of millions of persons were profiting from antimalaria activities, and the disease had been eliminated from a number of countries and territories where it was previously a health problem. There was need, however, for improvement in the quality of the administrative and technical services of some individual programmes. The Board therefore

urged the governments concerned to take the necessary steps for the training and provision of adequate technical and administrative personnel for the more effective prosecution of their eradication programmes, and asked national health authorities to strengthen the supervisory and epidemiological assessment activities of their malaria eradication services.

As of 18 January, the Malaria Eradication Special Account fell short by $1 300 000 of the amount required to finance the Organization's share in malaria eradication operations during 1960; a further $6 400 000 was required for operations in 1961. During the session of the Board, new contributions of 1 000 000 roubles ($250 000), in supplies and services, from the USSR, and A£15 000 ($35 000) from Australia were announced. It was also hoped that a contribution of DM1 000 000 ($238 000) would shortly be forthcoming from the Federal Republic of Germany. In addition the Government of Norway was prepared to make an initial contribution of $100 000 as soon as WHO could confirm that a sufficient number of other Member States would contribute relatively equivalent sums. Subsequently the Government of Canada notified its intention to seek the approval of Parliament for a contribution of US $100 000, the Government of Indonesia contributed $10 000, the Government of Tunisia $2000, and the Government of Denmark notified its intention of contributing Kr. 1 000 000 ($144 780), under conditions similar to those formulated by the Norwegian Government. The Board considered that continuing efforts should be made to finance the malaria eradication programme on a voluntary basis, and hoped that the economically more advanced countries would make substantial contributions to the fund. The attention of Member States was called to the need for support from individual governments in the effort to obtain contributions from industry and the general public.

BCG vaccination

A second evaluation report on BCG vaccination activities was presented to the Board in compliance with a resolution of the previous session. The conclusion drawn from this evaluation was that there was ample justification for the mass-scale use of BCG vaccination in the control of tuberculosis, even though it had been impossible to assess the exact part played by the vaccine in the reduction of morbidity and mortality from the disease, owing to, among a number of factors, the simultaneous employment of other control measures. The Board recommended that WHO continue to assist in the integration of BCG vaccination programmes with national tuberculosis control programmes and to study ways and means of evaluating the protective value of BCG vaccination.

Protection against radiation hazards

On the advice of one of the Sub-Committees of the Regional Committee for the Eastern Mediterranean, the Board examined the problem of the health implications of the atomic tests. During the discussions on this subject, some members of the Board stated that the Organization as a health agency had a great responsibility for the protection of man against possible damage from ionizing radiations, whatever their source. Some others recalled that the largest source of exposure at the present time is from X-ray and similar apparatus. The Board asked the Director-General to study the preventive aspects of reducing radiation hazards and present a report on the subject to the Thirteenth World Health Assembly, and included in the provisional agenda of the Assembly an item " Radiation health, including protection of mankind from ionizing radiation hazards whatever their source ".

Disarmament and funds for health

The Board considered a resolution on general and complete disarmament unanimously adopted by the United Nations General Assembly, and recommended that the Thirteenth World Health Assembly appeal to Member States to devote part of the funds which might be released by the implementation of this resolution to their health budgets,

"so as to improve the health of their population, mainly through the control of the most widespread diseases which claim large numbers of lives". It was also recommended that the Health Assembly ask the Director-General to submit to the Executive Board, as soon as agreement had been achieved on general and complete disarmament, proposals for the use of any resources resulting from such an agreement to meet urgent needs in the field of health.

Voluntary Fund for Health Promotion

It was recommended to the World Health Assembly that existing special accounts, with the exception of the Malaria Eradication Special Account, should be amalgamated into a single fund to be known as the Voluntary Fund for Health Promotion. This fund will include sub-accounts for smallpox eradication, medical research and community water supplies. During the session, a donation of $300 000 for the community water supply programme was announced by the Government of the United States of America.

Co-operation with UNICEF

The Board reviewed a report on activities jointly assisted by WHO and UNICEF. It noted with satisfaction that the UNICEF Executive Board had decided to continue support of the malaria eradication programme up to a ceiling of $10 million a year and to broaden its criteria for assistance to this programme, and expressed its satisfaction with the continuing close and effective collaboration between the two organizations.

World Health Year

The views of Member States and of the Regional Committees on the proposal to hold an International Health and Medical Research Year (or World Health Year) were reviewed by the Board. The Director-General was asked to make further efforts to obtain opinions on this subject from the considerable number of Member States which have not yet given them. It was suggested that the Thirteenth World Health Assembly in reconsidering the matter should provide for further study on the following points: the potential for health progress inherent in the idea, and the aims, organization, programme, timing, financing, etc. of the proposed activity.

Headquarters accommodation

The Board was informed of developments in connexion with the proposed new Headquarters building in Geneva. The site of the building—near the Palais des Nations, Geneva—has been placed at the disposal of the Organization by the authorities of the Republic and Canton of Geneva, who have also granted a loan of Sw. frs. 10 000 000 towards the cost of the building, the interest to be borne equally by the Canton and by the Organization. In addition, the Swiss Parliament has unanimously authorized an interest-free loan to WHO of Sw. frs. 20 000 000 for financing the construction of the new building.

Fifteen architects or architectural firms throughout the world have been asked to take part in the international competition for plans for the new building, and all have accepted. The competition is to close on 14 April 1960, and it is hoped to announce the results at the Thirteenth World Health Assembly.

WHO flag

The Board agreed to recommend to the Thirteenth World Health Assembly that an official WHO flag be adopted to be flown on the premises of the Organization and to be displayed elsewhere on ceremonial and other appropriate occasions. It was recommended that the design of this flag be based on the official emblem of the Organization, with or without modification.

Fourteenth World Health Assembly

It was decided to recommend to the Thirteenth World Health Assembly that the invitation of the Government of India to hold the Fourteenth World Health Assembly in New Delhi in 1961 be accepted.

Epidemiological and Statistical Information

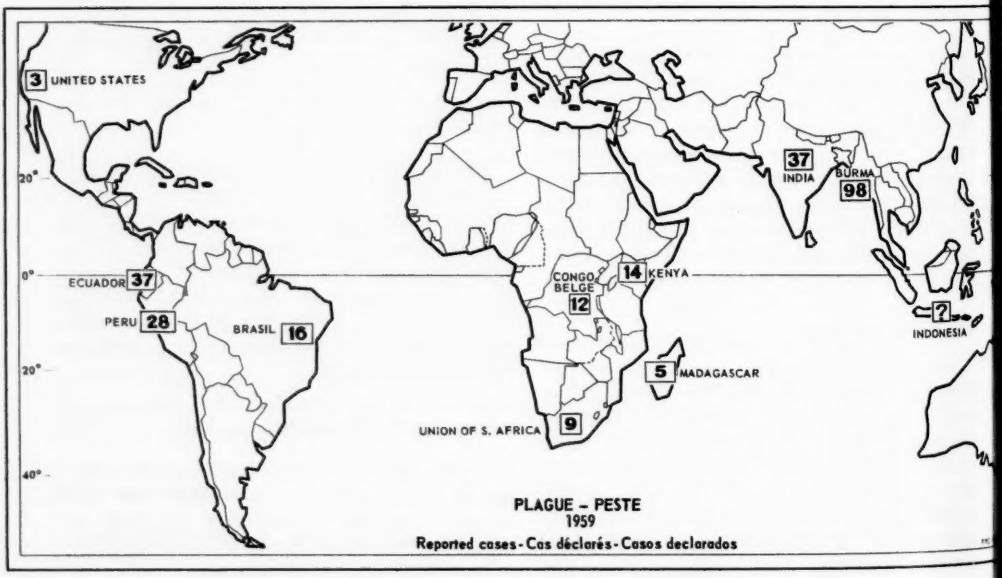
PLAGUE IN 1959

According to a recent number of the WHO *Weekly Epidemiological Record* (No. 4, 1960), the world incidence of plague in 1959 was as low as in 1958: less than 300 cases of human plague were officially reported in ten countries of Africa, America and Asia (excluding continental China). However, the occurrence of " accidental " single cases (United States of America and Madagascar) and of small foci in areas which were apparently free from human cases for one or more years (northern India, Union of South Africa) indicates that the infection is still maintained among rodents in wide areas of the three continents.

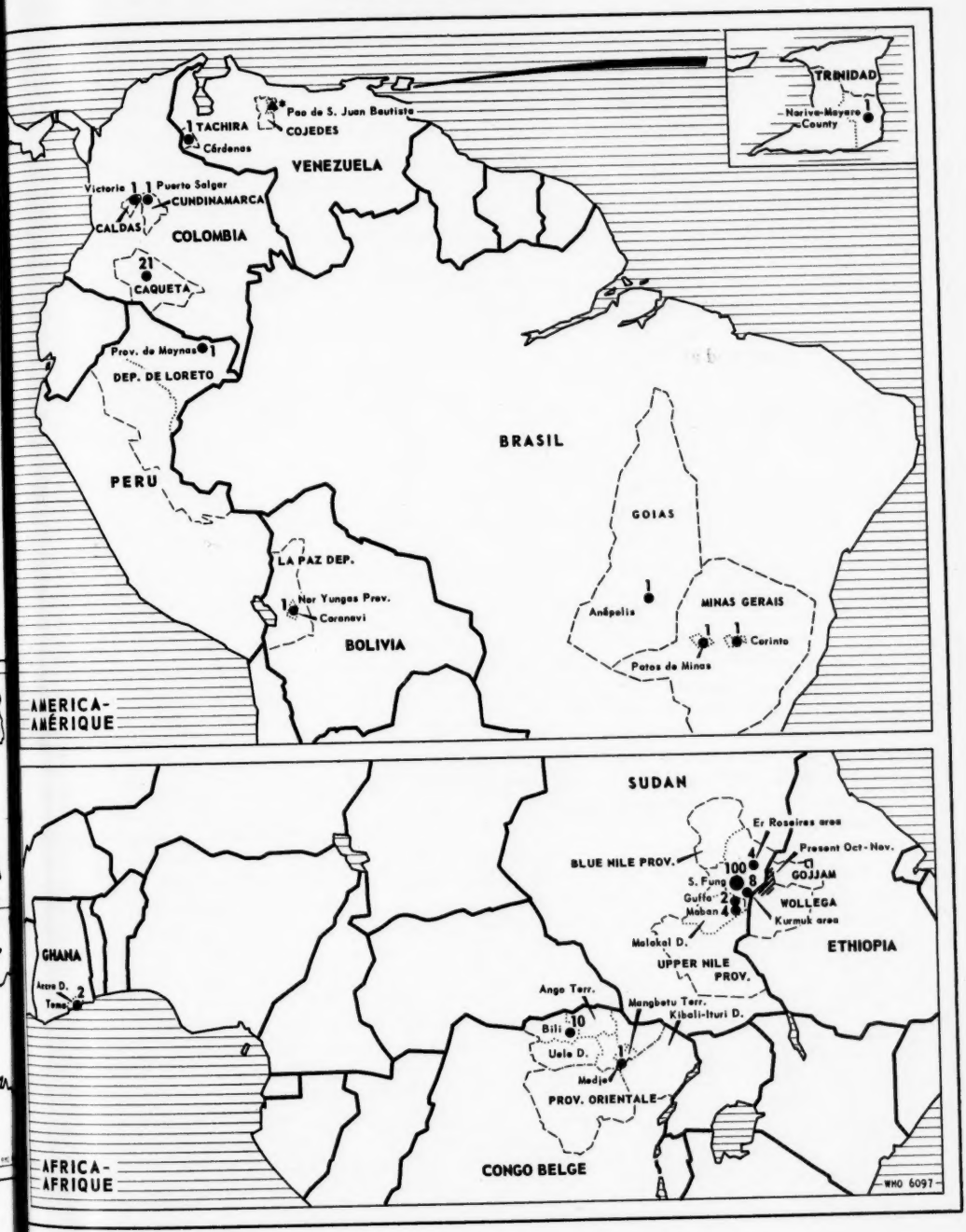
In Africa, cases were reported in the two areas which also notified cases in 1958, namely, the north-eastern part of the Belgian Congo and the Central Province of Kenya. In the Union of South Africa, an outbreak was reported in a district from which plague had apparently been absent since October 1957.

In America, there were active foci in Ecuador and Peru. In Brazil the disease was notified only in one area of the State of Bahia. Three single cases were notified in California and New Mexico in the United States of America.

In Asia, Burma notified the highest number of cases (98, including 36 in four inland urban areas).



YELLOW FEVER IN 1959



* *Yellow fever virus in a monkey*

YELLOW FEVER IN 1959

In Africa the presence of yellow fever was reported in an area where clinical cases had not been observed so far: the eastern part of the Sudan and neighbouring districts of Ethiopia. Altogether 118 cases and 87 deaths were recorded in this area. Eleven cases occurred during the year in the northern part of the Belgian Congo, and 2 in Ghana (see map on preceding page).

Official notifications in 1959 account for 31 cases of jungle yellow fever in America (as compared with 66 in 1958), including 23 in Colombia, 3 in Brazil, 2 in Trinidad (free from yellow fever since 1954), and single cases in Bolivia, Peru and Venezuela (see map). The presence of yellow fever virus in a vertebrate other than man (i.e., in a monkey) was demonstrated in Venezuela.

The above information is taken from the WHO *Weekly Epidemiological Record* (No. 5, 1960).

Reports of Expert Groups

Epidemiology of mental disorders *

In the past, psychiatry was primarily concerned with the individual. Towards the end of the nineteenth century, however, certain psychiatrists began to study mental disorders as mass diseases, concentrating at first on the genetic aspects of mental illness, but gradually taking environmental factors into account. Today it is realized that the prevention of mental disorder must be based on accurate knowledge of prevalence and incidence, i.e., that an "epidemiological" approach is required.

The eighth report of the WHO Expert Committee on Mental Health [1] reviews the uses of this approach in psychiatry and the most suitable methods for the different types of investigation involved.

The epidemiological approach in psychiatry can be used for two main purposes, which are to a certain extent inter-related: (*a*) to elicit facts about treated and untreated disease which are needed for the intelligent administration of community psychiatric services ("operational research"); (*b*) to discover those aspects of the habits, environment or organization of human populations which may affect the onset or course of mental disorders, and to assess their relative importance ("clinical research"). Since mental disorders differ in certain respects from other illnesses their epidemiological investigation presents a number of special problems. Thus, there are factors in psychiatric diseases which, because they belong to the sphere of values, cannot be fully quantified. Moreover, the etiology of mental disorder is more complex than that of most other types of illness, while there are considerable differences between various cultures in what is considered mentally abnormal.

One of the basic requirements of epidemiology is a generally accepted system of statistical classification which will allow data obtained by various investigators to be com-

* WHO Expert Committee on Mental Health (1960) *Eighth report: Epidemiology of mental disorders* (*Wld Hlth Org. techn. Rep. Ser.*, No. 185), 29 pages. Price: 1/9, $0.30, Sw. fr. 1.—. Also published in French and Spanish.

[1] Members of the Committee: Dr S. Btesh, Israel; Dr E. Essen-Möller, Sweden; Dr A. H. Leighton, USA (Rapporteur); Dr Tsung-yi Lin, China (Taiwan) (Rapporteur); Dr Ö. Ödegaard, Norway (Chairman); Dr P. D. Sivadon, France; Dr E. Stengel, United Kingdom (Vice-Chairman); Dr J. Vyncke, Belgian Congo. Secretariat: Dr D. Buckle, WHO Regional Office for Europe; Dr E. E. Krapf, WHO (Secretary); Dr Tigani el Mahi, WHO Regional Office for the Eastern Mediterranean; Dr J. S. Peterson, WHO; Dr Maria Pfister, WHO; Dr D. D. Reid, United Kingdom (Consultant).

pared. The lack of such a classification has repeatedly defeated attempts at comparing psychiatric observations and results of treatment, not only internationally but within one and the same country. Section V of the International Classification of Diseases, Injuries, and Causes of Death,[2] which deals solely with mental disorders, has been ignored or rejected in most countries; in fact, it has been widely used only in connexion with the classification of causes of death. The Committee agreed that, to be generally acceptable, a classification of mental disorders should use non-controversial concepts which are communicable in unambiguous terms and thus make for a high degree of comparability.

In view of the inadequacy and selective nature of most readily available mortality and morbidity data relating to mental illness, special surveys are nearly always essential in order to assess the needs for psychiatric care in an area, and the genetic, environmental and other circumstances which may precipitate the onset of such illness. The report reviews the problems of obtaining representative samples, of case finding, and of the standardization of psychiatric diagnosis in field surveys. The most standardizable, countable and comparable units of observation in psychiatry appear to be symptoms such as anxiety, depression, paranoid trends, excitement, delusions, hallucinations, and intellectual dullness. A list of such symptoms should therefore be established, together with a glossary and examples to make their meaning as clear as possible. Data could then be gathered from the population under study regarding the number, kinds and time of onset of these symptoms, and subsequently classified into syndromes and recognizable diagnostic entities such as pre-senile psychosis, schizophrenia, or manic-depressive psychosis.

In both operational and clinical research in the field of mental illness, the most pressing need is for the development of suitable technical methods and concepts. The Committee considered that there is a place for the deliberate controlled or designed experiment in the investigation of the etiology of mental disorder. Advantage might be taken of " experiments of opportunity " to observe the incidence of mental disorder among populations whose way of life has been radically altered by some act of nature or human activity beyond their control (e.g., disaster victims, refugees, etc.).

[2] World Health Organization (1957) *Manual of the International Statistical Classification of Diseases, Injuries, and Causes of Death, 1955 revision*, Geneva, p. 115

Appraisal of fellowships *

During the past decade, a vast amount of time, energy and money has been spent on the expansion of organized schemes to enable qualified persons to study abroad. To justify the continuation of such fellowship schemes and to ensure that the time and money are being used in the best possible way, adequate evaluation of the methods and results is essential. The report of the WHO Study Group on Appraisal of Fellowships [1] examines the problems confronting administrators planning appraisal of fellowship schemes in the field of health, and suggests criteria for appraisal.

As large-scale appraisals are expensive, it is unlikely that they will be made frequently, but many day-to-day procedures in organizing fellowship schemes should be subject to continual critical examination. A precise statement of the objectives of a fellowship is a prerequisite for any satisfactory appraisal. The questions asked in the appraisal must be

* WHO Study Group on Appraisal of Fellowships (1960) *Report* (*Wld Hlth Org. techn. Rep. Ser.*, No. 186), 15 pages. Price: 1/9, $0.30, Sw. fr. 1.—. Also published in French and Spanish.

[1] Members of the Study Group: Professor P. C. A. Antunes, Brazil (Chairman); Dr V. M. Coppleson, Australia; Mr L. Farrer-Brown, United Kingdom (Vice-Chairman); Dr R. H. Hazemann, France; Dr N. Jungalwalla, India; Dr H. W. Kumm, USA (Rapporteur); Dr B. Petrović, Yugoslavia. Representatives of United Nations agencies: Mr S. B. Bapat, UN; Mr H. Brixel, ILO; Mr H. Daniel, UN; Mr. A. Elliot, UNESCO; Mr J. de Martini, FAO. Secretariat: Dr M. Charnes, WHO Regional Office for the Americas; Miss L. M. Creelman, WHO; Dr W. Hobson, WHO Regional Office for Europe; Dr H. M. Kline, USA (Consultant); Dr D. A. Messinezy (WHO).

carefully chosen to elicit the information required, while eliminating subjective judgements as far as possible. Appraisals may be based on written evidence from the fellow's personal file, questionnaires, reports, etc., on the results of personal interviews, or on data obtained from field visits by selected persons. The report analyses the various methods and concludes that each has its values and its weaknesses; the choice of method will depend, therefore, on the nature of the fellowship programme and the type of appraisal planned.

Among the criteria of appraisal suggested are the choice and qualifications of fellows, the adequacy of the programme of study and of the administrative arrangements, the adjustment of the fellow to the conditions of study or training, his training record, and the results of his training, in terms of his subsequent employment and performance, his influence on the community, and benefits both to his own and the host country. Many aspects of appraisal are still in need of investigation. The report recommends the following subjects for further study: development of a series of case-histories of successful and unsuccessful fellowships; formulation of specific criteria for each stage of the fellowship process; evaluation of the fellow in his environment before and after the fellowship; placement of fellows; successes or failures of fellowships; and methodology of appraisals.

Biological standardization *

The WHO Expert Committee on Biological Standardization [1] has again examined a wide range of substances of importance in therapy, prophylaxis and diagnosis, and it reports the establishment of international reference preparations of amphotericin B, kanamycin, vancomycin, viomycin, human menopausal gonadotrophin, vitamin B_{12}, and egg lecithin, as well as international standards for antistreptolysin O, and swine erysipelas vaccine. Studies are under way with the aim of establishing international reference preparations of poliomyelitis vaccine, rabies vaccine, BCG vaccine, smallpox vaccine, anti-vaccinia gamma globulin, anti-leptospira sera and anti-yellow-fever serum. The Committee considered the need for international reference preparations of various enzymes that are in clinical use, such as streptokinase-streptodornase. It has not yet been possible to establish an international reference preparation of PAM, but in view of the extensive use of this preparation it was agreed that efforts should be continued to develop a more satisfactory method of evaluating the ability of PAM to provide a persistent concentration of penicillin in the blood.

A proposal to change the unit notation for penicillin was considered premature, but the National Institute for Medical Research, London, has been asked to propose for the next meeting an alternative definition of the International Unit of Penicillin, based on the weight of pure penicillin acid instead of on a standard preparation. In view of recent observations concerning the adsorption of purified tuberculin derivatives in high dilutions to the walls of vessels, there is an urgent need for redefinition of the International Unit of PPD, and a study is to be undertaken to determine whether it would be useful to replace the present international standard by a different preparation.

The report also outlines plans made by the Committee for establishing international reference preparations and international standards for a wide variety of diagnostic reagents in conjunction with the expanding activities of WHO in the field of medical research. It was recommended that in the first place

* WHO Expert Committee on Biological Standardization (1960) *Thirteenth report* (*Wld Hlth Org. techn. Rep. Ser.*, No. 187), 47 pages. Price: 1/9, $0.30, Sw. fr. 1.—. Also published in French and Spanish.

[1] Members of the Committee: Dr H. H. Cohen, Netherlands; Dr D. G. Evans, United Kingdom (Chairman); Dr N. H. Fisek, Turkey; Dr P. Krag, Denmark (Rapporteur); Dr D. C. Lahiri, India; Dr R. Murray, USA; Dr A. S. Outschoorn, Ceylon; Dr V. L. Troitski, USSR (Vice-Chairman). Representative of the Food and Agriculture Organization: Dr A. W. Stableforth, United Kingdom. Secretariat: Dr A. S. Benenson, USA (Consultant); Dr P. Bradstreet, United Kingdom (Consultant); Dr N. K. Jerne, WHO (Secretary); Mr J. W. Lightbown, United Kingdom (Consultant); Dr V. Soloviev, USSR (Consultant); Dr J. F. Winn, USA (Consultant).

work should be concentrated on sera used in the grouping and typing of viruses.

The list of International Standards and International Reference Preparations held for distribution at the International Laboratories for Biological Standards in Copenhagen and in London has been brought up to date and forms an annex to the report.

Addiction-producing drugs *

In its tenth report, the WHO Expert Committee on Addiction-Producing Drugs [1] recommended that eight new substances derived from different chemical groups and all having morphine-like effects should be subject to international control. These substances are allylprodine, benzethidine, furethidine, levophenacylmorphan, metazocine, norlevorphanol, phenazocine and piminodine.

The Committee felt that the fundamental criterion for the establishment and degree of control is the extent to which drug-induced behavioural disturbances are a risk to the community, for neither the chemical structure *per se* nor any definition, however descriptive, can be a complete guide indicating which substances should be placed under control. Consequently, there is a need for research along various lines in the field of drug addiction. In particular, to help the World Health Organization in carrying out its functions, the Committee must have at its disposal the results of basic and applied research in this field. But so far insufficient support has been forthcoming for such investigations. The Committee therefore strongly urged that research on drug addiction should be strengthened and expanded, since it continues to be a serious international public health problem.

The Committee made certain technical comments concerning the draft of the Single Convention on Narcotic Drugs. It expressed the view, *inter alia*, that only those preparations should be retained as exempted preparations which constitute no risk to public health and from which the potentially addicting agent is not readily recoverable.

* WHO Expert Committee on Addiction-Producing Drugs (1960) *Tenth report* (*Wld Hlth Org. techn. Rep. Ser.*, No. 188), 16 pages. Price: 1/9, $0.30, Sw. fr. 1.—. Also published in French and Spanish.

[1] Members of the Committee: Dr N. B. Eddy, USA; Dr L. Goldberg, Sweden (Chairman); Dr H. Isbell, USA (Vice-Chairman); Dr G. Joachimoglu, Greece; Dr J. La Barre, Belgium; Mr J. R. Nicholls, United Kingdom (Rapporteur); Dr V. V. Vassilieva, USSR; Dr V. Zapata Ortiz, Peru. Representatives of the United Nations: Mr A. Lande; Mr O. J. Braenden. Representative of the Permanent Central Opium Board and the Drug Supervisory Body: Mr L. Atzenwiler. Secretariat: Dr H. Halbach, WHO (Secretary).

Expert Committee on Leprosy *

Although the cause of leprosy is known and an effective treatment has been discovered, the disease still presents many unsolved problems. One of these is its degree of infectivity, which appears to depend on three factors as yet not fully assessed: the infectiousness of the individual patient, the susceptibility of the person exposed to infection, and the type of contact. Another is the classification of its many manifestations, an extremely controversial subject which may nevertheless be of crucial importance in the treatment and rehabilitation of patients.

These are two of the problems discussed by the WHO Expert Committee on Leprosy [1] in its second report. It examines the lepromin reaction, which is of established value for prognosis, for classification, and as a test of the individual's sensitivity to the leprosy bacillus;

* WHO Expert Committee on Leprosy (1960) *Second report* (*Wld Hlth Org. techn. Rep. Ser.*, No. 189), 27 pages. Price: 1/9, $0.30, Sw. fr. 1.—. Also published in French and Spanish.

[1] Members of the Committee: Dr J. A. Kinnear Brown, Uganda (Rapporteur); Dr Orestes Diniz, Brazil; Médecin-Colonel de Réserve P. Laviron, France (Vice-Chairman); Dr H. W. Wade, Philippines (Chairman); Dr R. V. Wardekar, India. Secretariat: Dr W. Bonne, WHO; Dr J. M. M. Fernández, Argentina (Consultant); Dr J. Gay-Prieto, WHO (Secretary); Dr V. Martínez-Domínguez, WHO.

the efficacy of BCG and chemotherapy in the prevention of leprosy; and present-day treatment and rehabilitation of patients. It outlines the organization of a campaign to reduce the incidence of leprosy, and stresses the need for proper training in and teaching of leprology and the education of the public about the disease.

A more extensive review of the Committee's work has already appeared in the January 1960 number of the *WHO Chronicle* (pages 21-22).

Notes and News

Hidden contacts with penicillin

There is already a vast literature on the dangers of the indiscriminate use of antibiotics for therapeutic purposes. Less well known are the possibilities of accidents in persons who have become sensitive to antibiotics to which they have found themselves exposed without even realizing it. These " hidden contacts ", as they are termed by Bernard B. Siegel, of the Allergy Division of the Department of Medicine, Jewish Hospital of Brooklyn, USA, are particularly common with penicillin, and are discussed in an article by Dr Siegel recently published in the WHO Bulletin.[1]

One of Dr Siegel's examples is of a physician who had previously experienced a severe reaction after an injection of penicillin, and who collapsed after drinking a glass of milk, emergency measures being required to bring him out of a state of shock. Later he experienced several other, though less severe, reactions immediately after drinking milk. Penicillin is much used in the USA for the treatment of cow mastitis, and has frequently been found in cow's milk in quantities sufficient to provoke allergic reactions in people who are sensitive to it.

Another example is of a nurse who had become sensitive to penicillin after several intramuscular injections. Later she was given an injection of testosterone with procaine hydrochloride for menstrual irregularity, and within a short time developed pruritus, itching of the throat, and generalized urticaria and angioneurotic oedema. Investigations showed that she was not sensitive to either the testosterone or the procaine, but had reacted to traces of penicillin left in the syringe. This girl had to give up nursing because she had itching of the eyes, nose and throat, swelling of the lips, and tightness of the chest whenever either she handled penicillin or it was used in her presence.

A third example is of a drug salesman who had experienced severe allergic shock immediately after taking a dose of medicine containing penicillin. A month later, while waiting in a doctor's consulting-room, he suddenly started to develop the same symptoms, at a time, it was discovered, when penicillin aerosol treatment was being given elsewhere in the consulting-room.

Generally sources of contact with penicillin are obvious, but these examples show that they may also be hidden. Another important hidden source is virus vaccines, which contain small amounts of penicillin antigen sufficient in some persons to cause allergic reactions. In view of the many hidden sources—Dr Siegel remarks—it would indeed be unwise to assume that anyone living in a modern community can escape contact with this antibiotic in one form or another. But because of the large numbers of potentially sensitive persons the greatest care should be taken to make this contact as slight as possible.

Water fluoridation in Chile

An experiment was undertaken at the end of 1953 to determine the effect of water fluoridation on the population of Curicó, Chile, and also to test the ability of local personnel to carry out fluoridation, study its effects and draw up a

[1] *Bull. Wld Hlth Org.*, 1959, **21**, 703

dental register. The concentration of fluorides was generally maintained around 1 p.p.m. (part per million), the widest variation being less than 20%. San Fernando, a town of the same type situated some 50 km away and comparable as regards population and social economy, was used as a control. At the beginning of the experiment, dental examinations were carried out in both towns.

In 1956, further dental examinations were carried out, using the same standards as in 1953. Over a period of two months, four dentists examined 4740 children, 3060 in Curicó, and 1680 in San Fernando.

On comparing the prevalence of caries in San Fernando in 1953 with the 1956 figure it was found that in general there were no significant changes. A similar comparison in Curicó revealed a distinct decrease. The data obtained in 1956 showed that in Curicó the prevalence of caries was less than that in San Fernando at all ages, and in particular up to the age of 6. The difference in favour of Curicó was 45% in children 3 years of age, 37% in those aged 4, and 15% in children aged 5. On studying the changes occurring during this period in each town, it became clear that in Curicó the percentage of children between 3 and 5 years of age who were free from caries had increased from 8.6 to 27 whereas in San Fernando the increase was only from 8.4 to 13.

In the opinion of the authors of an article recently published in the *Boletín de la Oficina Sanitaria Panamericana*,[1] the above investigations justify the conclusion that the cause of the very significant improvement in dental health in Curicó in 1956 was the consumption of drinking water containing 1 p.p.m. of fluorides by 90% of the population. The cost of fluoridation per person per year was estimated at 50 Chilean pesos, i.e., about US$0.05.

The hazards of eating raw fish

The Chinese liver fluke, *Clonorchis sinensis*, and the Oriental lung fluke, *Paragonimus westermani*, both cause endemic disease in the Republic of Korea. The former is common, and is considered to be the principal cause of the many cases of cirrhosis of the liver in Korea; the latter, though less widespread, has more serious effects, and is given a high ranking among public health problems. Just how much disease is caused by each has never been adequately estimated because surveys have been based on stool and sputum examinations, expensive and time-consuming techniques which do not guarantee that the eggs of the parasites, especially those of the lung fluke, are found. An intradermal test for these infestations was recently developed, however, by a US Army medical laboratory, and has been used in a preliminary survey of the prevalence of the diseases in certain provinces of Korea.

Both clonorchiasis and paragonimiasis, but especially the former, are widely prevalent among Korean adults, a discovery that conflicts with the previous view that they occur primarily in limited foci. In many areas, admittedly, the cases are probably not autochthonous: most of the people found in the survey to be positive reactors admitted to having travelled or lived in endemic areas and to having eaten raw fish there. The migration of the population southwards during the Korean war doubtless contributed greatly to the spread of the infestation. Among males the percentage of clonorchiasis is higher than among females, the reason for this probably being that men gather socially to drink rice wine and eat raw fish with it. Women are infrequent attenders at these gatherings, therefore much less exposed to infestation.

Paragonimiasis is usually thought to be caused by eating raw freshwater crab, but many Koreans with the disease denied doing this. In a large number of areas, too, the usual method of preparing uncooked crab includes heavy salting, and it is questionable whether the metacercariae could survive the three days in the brine that people deem necessary to give the crab a proper flavour. Perhaps—suggest the authors of an article on the survey in a recent WHO Bulletin[2]—the mode of infestation is to be sought elsewhere, as, for example, in the traditional home treatment of measles with the juice of crushed raw crayfish.

Proceedings of atomic energy conference

The Second United Nations Conference on the Peaceful Uses of Atomic Energy was held in

[1] *Bol. Ofic. sanit. panamer.*, 1959, 47, 412

[2] Walton, B. C. & Il Chyu (1959) *Bull. Wld Hlth Org.*, 21, 721

Geneva in September 1958, and the publication of its proceedings [1] is now complete. The 33 volumes, including an index, give a comprehensive account of the work being done all over the world on the manifold peaceful uses of atomic energy. The volumes contain a total of 19 000 printed pages and 15 000 illustrations, and their publication so soon after the Conference is a remarkable achievement.

Of particular interest to those concerned with the biological and medical aspects of the subject are: Volume 18, which deals with the treatment of atomic wastes and environmental aspects of atomic energy; Volume 21 on health and safety, giving biological standards relating to dosimetry, and measurement systems followed by nations engaged in atomic energy programmes; Volume 22 on the biological effects of radiation; Volume 23 on experience in radiological protection, containing details on occupational hazards of workers in atomic energy plants, and safety regulations; Volumes 24 and 25 on isotopes in biochemistry and physiology; Volume 26 on isotopes in medicine; and Volume 27 on isotopes in agriculture. The prices of these volumes range from $10.50, £3. 15s., or Sw. fr. 45 to $16.50, £5 18s., or Sw. fr. 70.

Training of sanitary inspectors

The fourth 10-week advanced training course for sanitary inspectors in the Philippines is now taking place in Pasig, Rizal Province. These courses were started by the Philippine Department of Health in June 1958 with the co-operation of the WHO Regional Office for the Western Pacific, the Philippine National Economic Council, and the US International Cooperation Administration (ICA). The technical adviser for the courses is Mr Gerard Murphy, a WHO sanitarian. The 1960 course is being attended by 29 sanitary inspectors from the principal municipalities in the Philippines; 85 sanitary inspectors were trained in the earlier courses. To accelerate the training programme and cover as many municipalities and provinces as possible, a second training centre is being planned in Baguio City with help from WHO.

Tenth international anaesthesiology course

The tenth anaesthesiology course, held under the auspices of the Danish Government and the WHO Regional Office for Europe, opened in Copenhagen on 26 January 1960. These courses started in 1950 and were at first planned for Scandinavian students only, but physicians from other countries were admitted, and to date they have been attended by a total of 254 physicians from 38 different countries. The 1960 course is being attended by 45 doctors from 21 countries in Europe, the Americas, Asia and the Eastern Mediterranean Region.

Details on the courses and on the work of the anaesthesiology centre in Copenhagen can be found in the March 1958 number of the Chronicle (page 69).

[1] United Nations (1958-1959) *Proceedings of the Second United Nations International Conference on the Peaceful Uses of Atomic Energy*, 33 volumes, Geneva

People and Places

Dental health in Thailand

Dr Robert Harris, Head of the Department of Preventive Dentistry of the University of Sydney, Australia, is at present paying a second visit to Thailand as WHO consultant in dental health. His first visit was in 1957 when he advised the Government on the development of dental education and dental services. During the present visit, which is largely in the nature of a " follow-up ", he will advise on the development of preventive dentistry.

Formerly Professor of Conservative Dentistry at the University of Otago, Dunedin, New Zealand, Dr Harris is editor of the *Australian Dental Journal* and has taken an active part in dental research in Australia.

Teaching of physiology in Cambodia

Under a programme of WHO assistance to the Royal School of Medicine, Phnom-Penh, Dr Ilse von Holten, from the Centre of Experimental Therapeutics, Hôpital de la Pitié, Paris, is at present spending three months in Cambodia to help the school establish a department of physiology. Funds and supplies for the programme—which aims at expanding the school's training facilities—are provided by the French Economic Mission, the US International Co-operation Administration (ICA), and United Nations Technical Assistance.

Born in Capetown, Union of South Africa, Dr von Holten obtained her diploma in physiology, chemistry and public health from the University of Stellenbosch and her doctorate in sciences from the University of Paris. After a period as lecturer in physiology at the University of Pretoria, South Africa, she returned to Paris to undertake experimental research on cardiac and cerebral physiology.

Inter-Regional Diarrhoeal Diseases Advisory Team

Dr Fred J. Payne has been appointed team leader and epidemiologist on the newly formed WHO Inter-Regional Diarrhoeal Diseases Advisory Team. In this capacity he visited Yugoslavia and several other eastern European countries in February. The other members of the team—including a bacteriologist and a paediatrician—will join Dr Payne later for intensive studies in the African Region.

Dr Payne received his medical training at the University of Pittsburgh and subsequently studied public health at the University of California. He has served with a dysentery unit on Koje Island, Korea, and as Chief of the United States Public Health Service Enteric Disease Investigations Unit. For the past two years he has been engaged in studies on the epidemiology of diarrhoeal diseases in the United States.

Maternal and child health appointment

Dr Marcèle Dorion, of Canada, has joined the staff of the maternal and child health programme which was undertaken in Tunisia in 1957 with the support of WHO and UNICEF. She will help in the expansion of the programme and in the training of professional and auxiliary personnel.

As consultant to the Quebec Department of Health, Dr Dorion has been responsible since 1954 for instructing the staff of 70 rural health units in maternal and child health. She has also done research on such public health problems as prematurity and hospital cross-infections.

Training centre for deaf-mutes

In 1958 a national training centre was established in Japan for early diagnosis and treatment of deaf-mutes, their occupational training, advice to their families, and education of the public on the subject. Dr M. F. Palmer, Professor and Head of Department of Logopedics, University of Wichita, Kans., USA, has been appointed by WHO to advise the Japanese Government on the further development of this centre.

Dr Palmer has more than twenty years' experience of teaching, clinical work and research in logopaedics.

Nutrition appointment

Dr D. M. Blankhart has been appointed WHO Inter-Regional Adviser on Nutrition for the Eastern Mediterranean and African Regions. He will advise the Regional Offices and national governments on all matters connected with nutrition, and especially on public health aspects. He will also collect information on nutrition and nutrition activities in the different countries in the Regions. A graduate of the University of Utrecht, Netherlands, Dr Blankhart was on the staff of the Nutrition Institute in Djakarta, Indonesia, prior to his appointment with WHO.

Population movements and malaria eradication

Mr R. M. Prothero is to visit Africa on behalf of WHO to study the relationship of population movements to problems of malaria eradication. His itinerary will include the Sudan and the Somaliland territories, as well as various parts of East and West Africa. He will also spend several days at the Rhodes-Livingstone Institute in Lusaka, Northern Rhodesia, where the subject of migration in Africa has been intensively studied.

Mr Prothero is a geographer by profession and a lecturer at the University of Liverpool, England. After teaching at Edinburgh University, he joined the staff of University College, Ibadan, Nigeria. There, while working with the West African

Institute of Social and Economic Research, he gained a close insight into many of the phenomena of migration.

Public health adviser for Cambodia

As part of its policy of helping governments strengthen their health administrations, WHO has appointed Dr Jacob Bierdrager as public health adviser to the Government of Cambodia. Dr Bierdrager will help the Government to co-ordinate its public health programmes, survey health conditions, and plan long-term national health programmes as the need arises. He will also co-ordinate WHO-assisted projects in Cambodia with the national health plan.

Born in the Netherlands, Dr Bierdrager received his basic medical training and later obtained his D.P.H. at the University of Amsterdam. For the past six years he has been Director of Health in Netherlands New Guinea.

Changes at WHO Headquarters

On 1 January 1960, a separate unit to deal with virus diseases was established in the Division of Communicable Diseases. Dr A. M.-M. Payne, formerly Chief Medical Officer, Endemo-Epidemic Diseases, is now Chief Medical Officer, Virus Diseases. Dr N. Ansari has succeeded Dr Payne as Chief Medical Officer, Endemo-Epidemic Diseases.

Also on 1 January 1960, the functions relating to the organization of medical care were detached from the Social and Occupational Health unit and Dr A. L. Bravo—previously Chief Medical Officer, Social and Occupational Health—became Chief Medical Officer, Organization of Medical Care.

The new Chief Medical Officer, Social and Occupational Health, is Dr M. O. Shoib, of the United Arab Republic. Before taking up this appointment at WHO Headquarters, Dr Shoib was in charge of the Callioub Demonstration and Training Centre, Visiting Professor and Head of the Department of Occupational Health, High Institute of Public Health, Alexandria, and examiner in public health at the University of Ein Shams, Cairo, and Alexandria University. He was educated at Cairo, Harvard and Columbia Universities.

Review of WHO Publications

TUBERCULOSIS

Bulletin of the World Health Organization, 1960, Volume 22, Number 1-2 (pages 1-196)

In earlier numbers of the Bulletin several reports have been published showing that micro-organisms other than tubercle bacilli, and as yet unidentified, may be responsible for the low-grade tuberculin sensitivity observed in certain parts of the world. The first paper in this number, by Nyboe, gives a comprehensive analysis of the results of tuberculin testing carried out by WHO research and survey teams in a total of 33 countries during the last ten years. The data confirm that the low-grade tuberculin sensitivity is distributed according to a striking geographical pattern: in countries with a temperate or sub-tropical climate the reactions to a low dose of tuberculin are of two different kinds—clearly positive or clearly negative—whereas in tropical lowlands a large proportion of the reactions are of intermediate size. This distinct epidemiological pattern may provide a clue to the etiology of such reactions. The practical implication of this finding is that in tropical countries a clear-cut distinction between persons infected with tubercle bacilli and those not infected can hardly be made by means of the present tuberculin test. The selection of persons for BCG vaccination is therefore difficult in these countries and the diagnostic value of the tuberculin test is low.

Tuberculosis is supposed often to result from a household infection, and " contacts " of tuberculous patients are usually given special attention in tuberculosis control programmes. In the second paper in this issue, Andersen & Geser have

made an examination of the tendency for infection in children to be accumulated within particular households, using data from a number of WHO tuberculosis prevalence surveys in Africa. Only persons with strong allergy were counted as positive reactors, so as to avoid the inclusion of too many persons with low-grade, " non-specific " sensitivity.

The results show that although there is a statistically significant tendency for positive reactors to accumulate in certain households, this tendency is surprisingly weak; only a modest proportion of all infected children seem to have acquired infection within their own households. The authors discuss the practical implications of their findings in detail and conclude that it would scarcely be justifiable in the countries and populations examined to concentrate tuberculosis control measures on households with many tuberculin positive children, perhaps not even on households with known cases of infectious tuberculosis, because such households seem to represent only a small fraction of the total tuberculous infection and disease in the community.

WHO recommends that a tuberculosis programme in a less-developed country should include, at a certain stage, the establishment of a national pilot area project. Dr Frimodt-Møller's report on a community-wide tuberculosis study in Madanapalle, India, describes such a project covering a population of 60 000 with a high prevalence of low-grade tuberculin sensitivity and, as it turned out, with a rather low prevalence of tuberculosis. This population was followed between 1950 and 1955 with annual X-ray and tuberculin testing and the hospitalization of infectious cases. During this period the mortality from tuberculosis was reduced rather dramatically, presumably because of treatment with antituberculosis drugs, but the prevalence of tuberculosis seemed unchanged. The author concludes that even with active and planned efforts quick results in controlling or eradicating tuberculosis can scarcely be expected in a community like the one described.

The paper also reports on a BCG trial that gave very disappointing results, in terms of both allergy and immunity in the vaccinated persons. Although the most obvious among the possible explanations of this is that a severely attenuated vaccine was used in the trial, the findings also raise once more the important question whether persons with low-grade (presumably " non-specific ") tuberculin sensitivity already possess a certain degree of acquired immunity.

The transport of vaccine in tropical regions presents considerable difficulty owing to the vulnerability of liquid BCG vaccine to exposure to heat and to light. The fourth paper in this issue, by Geser & Azuma, deals with the effects of storage of Japanese freeze-dried glutamate BCG vaccine at higher temperatures on its allergenic potency in human beings. Whereas liquid vaccine was seriously damaged after one month's storage at 30°C, the allergenic potency of the freeze-dried glutamate vaccine was not much altered after one month at 42°C. The duration of the allergy induced by such heat-treated vaccine and other problems concerning the use of freeze-dried BCG vaccine are still under study.

One of the several methods in common use for assessing the biological activity of BCG vaccines is the vaccination and subsequent tuberculin testing of guinea-pigs. The last two papers in this issue, by Tolderlund, Bunch-Christensen & Waaler, give a detailed account of the allergic response in guinea-pigs to BCG vaccine—an account intended to provide a basis for the future use of this method. One paper is concerned with the duration of allergy after vaccination with standard strength vaccine and more particularly with the effect of the tuberculin test itself on the animal's ability to react to subsequent tuberculin tests. The authors demonstrate that allergy is apparent after as little as one week, reaches a maximum after 1-2 months, remains stable for about one month, then begins to decrease steadily, and has practically disappeared after 12 months. This, however, is true only if each animal is tested not more than once after vaccination; with repeated tests in the same animal there is practically no waning of allergy, even one year after vaccination. This has been demonstrated in the present studies by giving one half of the animals an extra tuberculin test two weeks before the test for the final evaluation of allergy. Thus the tuberculin test has a " boosting " effect on waning allergy though not on the allergy at its maximum strength.

In the last paper, the development and course of allergy are examined not only for standard strength vaccine, but also for tenfold dilutions

thereof, down to dilutions so thin that they contain on average less than one viable unit per dose. To avoid the " boosting " effect of tuberculin, each animal was tested only once.

It was seen that diluted vaccine (down to 1/10 000 of standard strength) gives an allergy that develops late, yet becomes nearly as strong as that after standard strength vaccine 10-12 weeks after vaccination. With greater dilution of the vaccine, few or no animals became allergic. But even with the very weak doses of vaccine, the guinea-pig either becomes allergic and then ultimately rather strongly allergic, or else remains quite anergic. This is in striking contrast to the response to BCG in human beings, in whom the strength of allergy depends on the size of the dose of BCG.

These findings no doubt necessitate a reconsideration of the use of allergy in guinea-pigs for assays of BCG. An assay method should allow of differentiation between strong and weak vaccines; more particularly, the measurement of allergy in animals should make it possible to predict the allergenic potency in man. Apparently, a tuberculin test in a vaccinated guinea-pig does neither.

VIRUS DISEASES

Bulletin of the World Health Organization, 1960, Volume 22, Number 3-4 (pages 197-438)

Virology today is at the same stage as bacteriology was at the beginning of the twentieth century. New pathogenic organisms are constantly being discovered, methods of culture and investigation are being improved, protective measures are being worked out and becoming established practice. As the " biology " of viruses grows more complex and refined, so do research techniques become finer and more precise. The ingenuity of a host of research workers is being put to the test by the antigenic lability of the viruses, by their existence in masked forms in reservoir hosts (still mostly unknown), where they escape current methods of investigation, and by our ignorance of the pathogenicity of many of those found in man and beast. One of the chief tools of virological research is serology. Because viruses stimulate the formation of specific antibodies in the body, vaccination ensures some degree of protection and opens the door to an effective means of combating the diseases they cause. Epidemiology based on serological investigation also makes it possible now to study the distribution of viruses and virus diseases on a world scale, through the traces they leave in populations in the form of antibodies.

Most of the articles in the issue of the Bulletin under review deal with live poliovirus vaccination; these are discussed elsewhere in the present Chronicle (see page 137).

Although poliomyelitis is still very much to the fore, other enteric viruses are becoming of increasing importance. Those which cause diarrhoea, and the enormous group of " orphan " viruses, whose etiology is as yet obscure, form a fresh group of infectious organisms; there are the ECHO viruses in man, and similar viruses found in animals which are designated—according to the animal harbouring them—by such abreviations as ECCO, ECMO, ECBO and so forth.

In his general review of " orphan " viruses, Kalter describes the types found in animals and methods of isolating them, and touches on theories about the nature of the " masked " forms in which they appear. One of the difficulties encountered in the identification and isolation of viruses in tissue cultures arises from the presence in explants of masked viruses which may display cytopathogenic activity in serial cultures and so prevent identification of the viruses sought.

Culture contamination is studied in greater detail by Tobin, in a note on the possible presence of monkey viruses pathogenic to man in tissue cultures of monkey kidney. The author stresses the drawbacks their presence may have in cultures used for the production or checking of poliomyelitis vaccines and the risks of laboratory infection to research workers.

In a general review of the ecology and etiology of the arthropod-borne encephalitides, Miles discusses the work done on virus transmission cycles, on reservoir hosts (birds and animals), and on the seasonal and climatic conditions favouring epidemics of encephalitis.

The laboratory or field diagnosis of virus diseases can be made easier by a simplified

variation of the plaque-inhibition test, here described by Porterfield. It is particularly applicable to epidemiological research on yellow fever, and enables new viruses to be discovered.

Serum-and-vaccine treatment of rabies is still under trial. Veeraraghavan & Subrahmanyan assess the effectiveness of this method of treatment against challenges of increasing severity, and consider that it is superior to treatment with vaccine alone only at a challenge of 50 LD_{50} and above, being fully effective at challenges of between 100 and 300 LD_{50}. No treatment is effective against a higher challenge and none gives 100% protection.

The application of tissue culture techniques to the study of rabies virus has met with limited success. M. M. Kaplan and his colleagues report progress in the cultivation of rabies fixed virus in explants of hamster kidney tissue and demonstrate that cultured virus can be stained by means of the fluorescent antibody technique.

Smallpox vaccine is the subject of two papers. In one, C. Kaplan compares two methods of vaccinia virus titration—intravenous injection of chick embryos, and pock-counting on the chorioallantoic membrane of chick embryos. The intravenous injection method is lengthy, and differences of virulence may falsify comparisons between the results obtained by this method and those obtained by the pock-counting method, into which the virulence factor does not enter.

The deterioration of smallpox vaccine at different temperatures can be assessed by the accelerated degradation test, described in a note by Fisek.

The influenza pandemic of 1957-58 was observed in particularly favourable conditions in the Netherlands, where it began at a time when the incidence of respiratory infections was at its minimum. Its course and seriousness could therefore be gauged with a fair degree of accuracy. Mulder & Masurel give an account of the pandemic, discuss the conditions which probably favoured the spread of the influenza wave, and note the persistence of the virus in the population several months after the end of the epidemic.[1]

When influenza is diagnosed serologically by the haemagglutination-inhibition test the presence of non-specific inhibitors may falsify the results. Ananthanarayan & Paniker discuss these inhibitors, showing that they are present in the normal sera of man and animals, and describe the qualitative and quantitative differences between them. They conclude that no technique for the destruction of the inhibitors can be effective in all cases, and recommend the combination of several techniques.[2]

Gibiński et al. describe an epidemic of Bornholm disease in Upper Silesia, which showed a change within a short space of time in the group of Coxsackie virus circulating among the population.

[1] A summary of this article appeared in *WHO Chronicle*, 1960, **14**, 83.

[2] A summary of this article appeared in *WHO Chronicle*, 1960, **14**, 122.

International Non-Proprietary Names for Pharmaceutical Preparations

In accordance with paragraph 3 of the Procedure for the Selection of Recommended International Non-Proprietary Names for Pharmaceutical Preparations,[1] notice is hereby given that the following names are under consideration by the World Health Organization as proposed international non-proprietary names.

Comments on, or formal objections to, the proposed names may be forwarded by any person to the Pharmaceuticals unit of the World Health Organization within four months from 1 April 1960.

The inclusion of a name in the lists of proposed international non-proprietary names does not imply any recommendation for the use of the substance in medicine or pharmacy.

PROPOSED INTERNATIONAL NON-PROPRIETARY NAMES (*Prop. I.N.N.*): LIST 9 [2]

Proposed International Non-Proprietary Name (Latin, English)	*Chemical Name or Description*
allylprodinum allylprodine	3-allyl-1-methyl-4-phenyl-4-propionoxypiperidine
benzethidinum benzethidine	1-(2-benzyloxyethyl)-4-phenylpiperidine-4-carboxylic acid ethyl ester
furethidinum furethidine	1-(2-tetrahydrofurfuryloxyethyl)-4-phenylpiperidine-4-carboxylic acid ethyl ester
levophenacylmorphanum levophenacylmorphan	(-)-3-hydroxy-N-phenacylmorphinan
metazocinum metazocine	1,2,3,4,5,6-hexahydro-8-hydroxy-3,6,11-trimethyl-2,6-methano-3-benzazocine
norlevorphanolum norlevorphanol	(-)-3-hydroxymorphinan
phenazocinum phenazocine	1,2,3,4,5,6-hexahydro-8-hydroxy-6,11-dimethyl-3-phenethyl-2,6-methano-3-benzazocine
piminodinum piminodine	1-(3-phenylaminopropyl)-4-phenylpiperidine-4-carboxylic acid ethyl ester

[1] *Off. Rec. Wld Hlth Org.*, 1955, **60**, 3, 55

[2] Other lists of proposed international non-proprietary names can be found in *Chron. Wld Hlth Org.*, 1953, **7**, 299; 1954, **8**, 216, 313; 1956, **10**, 28; 1957, **11**, 231; 1958, **12**, 102; *WHO Chronicle*, 1959, **13**, 105, 152.

CORRIGENDA

Vol. 13, No. 12

INTERNATIONAL NON-PROPRIETARY NAMES FOR PHARMACEUTICAL PREPARATIONS

p. 465, chemical formula for " carbinoxaminum "

delete chorophenylmethane
insert chlorophenylmethane

p. 466, chemical formulae for " cycriminum " and " dioxethedrinum ", in each case

delete . . . propan-1-01
insert . . . propan-1-ol

p. 467, twelfth name (Latin)

delete fludroxortisoni
insert fludrocortisoni

p. 467, chemical formula for " hexylcainum "

delete 2-prophyl
insert 2-propyl

p. 471, fifteenth name (Latin)

delete phthalysulfamethizolum
insert phthalylsulfamethizolum

TUBERCULOSIS

The efficacy of the tuberculin test: an analysis based on results from 33 countries—*Jørgen Nyboe*

The distribution of tuberculous infection among households in African communities—*Stig Anderson & Anton Geser*

A community-wide tuberculosis survey in a South Indian rural population, 1950-55—*J. Frimodt-Møller*

Further studies on the heat-stability of freeze-dried glutamate BCG vaccine: effect of storage at 30°-50°C on allergenic potency in humans—*Anton Geser & Yoshikuni Azuma*

Development and duration of BCG-induced allergy in the guinea-pig—*Knud Tolderlund, Kirsten Bunch-Christensen & Hans Waaler*

Development and course of tuberculin allergy in guinea-pigs vaccinated with various doses of Danish liquid BCG vaccine—*Knud Tolderlund, Kirsten Bunch-Christensen & Hans Waaler*

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